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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action *After the Filing of an Appeal Brief*	Application No. 10/038,260	Applicant(s) NASH ET AL.	
	Examiner Phuong Huynh	Art Unit 1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

The reply filed 07 February 2005 is acknowledged.

1. ☐ The reply filed on or after the date of filing of an appeal brief, but prior to a final decision by the Board of Patent Appeals and Interferences, will not be entered because:

   a. ☐ The amendment is not limited to canceling claims (where the cancellation does not affect the scope of any other pending claims) or rewriting dependent claims into independent form (no limitation of a dependent claim can be excluded in rewriting that claim). See 37 CFR 41.33(b) and (c).

   b. ☐ The affidavit or other evidence is not timely filed before the filing of an appeal brief. See 37 CFR 41.33(d)(2).

2. ☐ The reply is not entered because it was not filed within the two month time period set forth in 37 CFR 41.39(b), 41.50(a)(2), or 41.50(b) (whichever is appropriate). Extensions of time under 37 CFR 1.136(a) are not available.

   Note: This paragraph is for a reply filed in response to one of the following: (a) an examiner's answer that includes a new ground of rejection (37 CFR 41.39(a)(2)); (b) a supplemental examiner's answer written in response to a remand by the Board of Patent Appeals and Interferences (37 CFR 41.50(a)(2)); or (c) a Board of Patent Appeals and Interferences decision that includes a new ground of rejection (37 CFR 41.50(b)).

3. ☒ The reply is entered. An explanation of the status of the claims after entry is below or attached.

4. ☒ Other: *The new matter rejection of claims 5, and 32-38 is hereby withdrawn in view of amendment filed 2/7/05. Claims 1, 3 and 5-38 are pending and are on appeal.*

The Issues on appeal are as follow:
A. Whether Claims 1, 3 and 5-38 are unpatentable under 35 USC 112 because the specification does not enable a person skilled in the art to which it pertains to make and use the invention.
B. Whether Claims 1, 3 and 5-38 are unpatentable under 35 USC 112 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.
C. Whether Claims 1 and 3 are indefinite for failing to particularly point out and distinctly claim the subject matter which Appellants regard as the invention.
D. Whether Claims 1, 3, 5, 8, 11, 14 and 17 are unpatentable under 35 USC 103(a) over U.S. Patent No. 5,080,895 (Tokoro) in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Krause et al and Trinchieri et al.
E. Whether Claims 1, 3, 5, 8, 11, 14 and 17 are unpatentable under 35 USC 103(a) over Yokoyama et al in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Krause et al and Trinchieri et al.
F. Whether Claims 5, 20, 23 and 26 are unpatentable under 35 USC 103(a) over U.S. Patent No. 5,080,895 (Tokoro) in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Krause et al, Trinchieri et al, U.S. Patent No. 4,748,018 (stolle et al) and Sugita-Konishi et al.
G. Whether Claims 5, 20, 23 and 26 are unpatentable under 35 USC 103(a) over Yokoyama et al in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Krause et al, Trinchieri et al, U.S. Patent No. 4,748,018 (stolle et al) and Sugita-Konishi et al.
H. Whether Claims 6, 7, 9-10, 12-13, 15-16, 18-19 and 29-38 are unpatentable under 35 USC 103(a) over U.S. Patent No. 5,080,895 (Tokoro) in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Krause et al, Trinchieri et al, U.S. Patent No. 6,086,878 (Adalsteinsson et al) and U.S. Patent No. 4,166,867 (Betz et al).
I. Whether Claims 6, 7, 9-10, 12-13, 15-16, 18-19 and 29-38 are unpatentable under 35 USC 103(a) over Yokoyama et al in view of Kaspers et al, Krause et al, U.S. Patent No. 5,471,489 (pimental), Trinchieri et al, U.S. Patent No. 6,086,878 (Adalsteinsson et al) and U.S. Patent No. 4,166,867 (Betz et al).
J. Whether Claims 20-28 and 38 are unpatentable under 35 USC 103(a) over U.S. Patent No. 5,080,895 (Tokoro) in view of Kaspers et al, U.S. Patent No. 5,471,489 (pimental), Trinchieri et al, U.S. Patent No. 6,086,878 (Adalsteinsson et al), U.S. Patent No. 4,166,867 (Betz et al) and Sugita-Konishi et al.
K. Whether Claims 20-28 and 38 are unpatentable under 35 USC 103(a) over Yokoyama et al in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Trinchieri et al, U.S. Patent No. 6,086,878 (Adalsteinsson et al), U.S. Patent No. 4,166,867 (Betz et al) and Sugita-Konishi et al.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/038,260
Filing Date: January 07, 2002
Appellant(s): NASH ET AL.

Richard John Bartz
For Appellant

SUPPLEMENTAL EXAMINER'S ANSWER

This supplemental examiner's answer is in response to the appeal brief filed 9/23/04, and the subsequent amendment filed 2/7/05.

This examiner's answer is also in response to the reply brief filed 2/17/05 and to correct the listing of prior art of record on page 4 last line of the Examiner's Answer mailed 12/17/04.

Other than correcting the listing of prior art of record and the reducing the number of issues on appeal, the examiner's answer remains the same.

Appellants' reply Brief filed 2/17/05 should have been under 37 CFR 41.41 instead of 37 CFR 1.193.

In response to Appellants' statement that an amendment has been filed 2/7/05 and no response has been received, please see enclosed Advisory Action. The amendment has been entered. The new matter rejection of claims 5 and 32-38 has been withdrawn in view of the amendment filed 2/7/05 to remove the term "living being".

In response to Appellants' argument on page 5 of the reply brief filed 2/17/05 that the examiner's analysis of Yokoyama et al publication does not agree with the disclosure of this publication (Yokoyama et al, Vaccine 16(4): 338-393, Feb 1998), there is no reference to piglets. Only egg yolk immunoglobulin was used in the experiment. It is noted that the rejection of claims 1, 3, 5, 8, 11, 14, and 17 were rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,080,895 (Tokoro et al, of record, Jan 1992; PTO 1449) or Yokoyama *et al* (Infection and Immunity 60(3): 998-1007, March 1992; PTO 892) each in view of Kaspers *et al* (Zentralbl Veterinarmed A 43(4): 225-31, June 1996; PTO 892), US Pat No 5,741,489 (Pimentel et al, of record, April 1998; PTO 1449), Krause *et al* (of record, Appl Environ Microbiol 62(3): 815-21; 1996, PTO 892), and Trinchieri *et al* (Urol Res 18(5): 305-8, 1990; PTO 892). (see page 9 last paragraph of Examiner's answer mailed 12/17/04). The publication of Yokoyama reference is Infection and Immunity 60(3): 998-1007, March 1992, not Vaccine 16(4): 338-393, Feb 1998 as argued. However, Appellants are correct that the listing of prior art of record on page 4, last line of the previous Examiner's answer should have been Yokoyama et al, Infection and Immunity 60(3): 998-1007, March 1992 instead of Yokoyama et al, Vaccine 16(4): 338-393, Feb 1998. The Yokoyama et al reference, Infection and Immunity 60(3): 998-1007, March 1992, was cited on PTO 892 mailed to Appellants on 2/13/04.

In response to Appellants argument that there is no reference to piglets, Yokoyama et al teach a method of producing a microbial adherence inhibitor such as IgY for administration to food animal such as piglets to inhibit the adherence of a targeted colony forming immunogen such as *E coli* in the intestinal tracts of neonatal piglets (see abstract, in particular).

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is incorrect.

The amendment filed on August 27, 2004 has been entered. The response to said amendment was mailed October 6, 2004.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows: The rejection of Claims 1, 3 and 5-38 under the judicially created doctrine of obviousness-type double patenting is hereby withdrawn in view of the restriction in the parent application Serial No. 09/616,843. It is noted there is a typographical error in the claims of Issue C. The correct rejected claims are provided below.

The Issues on appeal are as follow:

A. Whether Claims 1, 3 and 5-38 are unpatentable under 35 USC 112 because the specification does not enable a person skilled in the art to which it pertains to make and use the invention.

B. Whether Claims 1, 3 and 5-38 are unpatentable under 35 USC 112 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

C. Whether Claims 1 and 3 are indefinite for failing to particularly point out and distinctly claim the subject matter which Appellants regard as the invention.

D. Whether Claims 1, 3, 5, 8, 11, 14 and 17 are unpatentable under 35 USC 103(a) over U.S. Patent No. 5,080,895 (Tokoro) in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Krause et al and Trinchieri et al.

E. Whether Claims 1, 3, 5, 8, 11, 14 and 17 are unpatentable under 35 USC 103(a) over Yokoyama et al in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Krause et al and Trinchieri et al.

F. Whether Claims 5, 20, 23 and 26 are unpatentable under 35 USC 103(a) over U.S. Patent No. 5,080,895 (Tokoro) in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Krause et al, Trinchieri et al, U.S. Patent No. 4,748,018 (Stolle et al) and Sugita-Konishi et al.

G. Whether Claims 5, 20, 23 and 26 are unpatentable under 35 USC 103(a) over Yokoyama et al in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Krause et al, Trinchieri et al, U.S. Patent No. 4,748,018 (stolle et al) and Sugita-Konishi et al.

H. Whether Claims 6, 7, 9-10, 12-13, 15-16, 18-19 and 29-38 are unpatentable under 35 USC 103(a) over U.S. Patent No. 5,080,895 (Tokoro) in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Krause et al, Trinchieri et al, U.S. Patent No. 6,086,878 (Adalsteinsson et al) and U.S. Patent No. 4,166,867 (Betz et al).

I. Whether Claims 6, 7, 9-10, 12-13, 15-16, 18-19 and 29-38 are unpatentable under 35 USC 103(a) over Yokoyama et al in view of Kaspers et al, Krause et al, U.S. Patent No. 5,471,489 (pimental), Trinchieri et al, U.S. Patent No. 6,086,878 (Adalsteinsson et al) and U.S. Patent No. 4,166,867 (Betz et al).

J. Whether Claims 20-28 and 38 are unpatentable under 35 USC 103(a) over U.S. Patent No. 5,080,895 (Tokoro) in view of Kaspers et al, U.S. Patent No. 5,471,489 (pimental), Trinchieri et al, U.S. Patent No. 6,086,878 (Adalsteinsson et al), U.S. Patent No. 4,166,867 (Betz et al) and Sugita-Konishi et al.

K. Whether Claims 20-28 and 38 are unpatentable under 35 USC 103(a) over Yokoyama et al in view of Kaspers et al, U.S. Patent No. 5,741,489 (pimental), Trinchieri et al, U.S. Patent No. 6,086,878 (Adalsteinsson et al), U.S. Patent No. 4,166,867 (Betz et al) and Sugita-Konishi et al.

(7) Grouping of Claims

Appellant's brief includes a statement that the claims fall into three groups. Group I (claims 1, 3, 5, 8, 17, 20, 23 and 26), Group II (claims 9-10, 12-13, 15-16, 18-19, 21-22, 24-25 and 27-28 which include the subject matters of claims 8, 11, 14, and 17) and Group III (claims 6-7, and 29-38) do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

However, the appellant's statement in the brief that the claims of Groups I, II and III do not stand or fall together is not agreed with because the method of producing microbial inhibitor in Group II (claims 9-10, 12-13, 15-16, 18-19, 21-22, 24-25 and 27-28) and Group III (claims 6-7, and 29-38) require the same IgY antibody as the microbial adherence inhibitor in Group I (claims 1, 3, 5, 8, 17, 20, 23 and 26). Further, coating dry feed carrier with said antibody in groups II and III is irrelevant to the method of producing the immunoglobulin as the microbial adherence inhibitor. Therefore, claims 1, 3 and 5-38 should stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

5,080,895	Tokoro	1-1992
5,741,489	Pimentel	4-1998
4,748,018	Stolle	5-1988
6,086,878	Adalsteinsson	07-2000
4,166,867	Betz	9-1979

Kuby et al, Immunology, second edition, pages 85-96, 1994.

Abaza et al, J of Protein Chemistry 11(5): 433-444, 1992.

Stryer et al, in Biochemistry, Third edition, W H Freeman Company, New York, pages 31-33, 1998.

Yokoyama et al, Infection and Immunity 60(3): 998-1007, March 1992.

Kaspers et al, Zentralbl Veterinarmed A 43(4): 225-31, June 1996.

Krause et al, Applied and Environmental Microbiology,Vol. 62, no. 3 (Mar 1996), page 815-821.

Trinchieri et al, Urol Res 18(5): 305-8, 1990; Abstract.

Sugita-Konishi et al, Biosci Biotechnol Biochem 60(5): 886-8, May 1996.

(10) Grounds of Rejection

The following grounds of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112 first enablement

Claims 1, 3, and 5-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a method for the production of a microbial adherence inhibitor in the form of IgY for administration to food animals to inhibit the adherence of targeted colony-forming bacteria in the rumen or intestinal tracts of said food animal wherein the colony-forming bacteria are selected from the group consisting of *P. anaerobius, C. sticklandii, C. aminophilium, E. coli, Listeria, Salmonella* and *Campylobacter* which method comprises inoculating female chickens, in or about to reach their egg laying age, with said colony-forming bacteria; allowing a period of time sufficient to permit the production in the bird of antibody to said targeted immunogen; Harvesting the eggs laid by the birds; Separating the antibody-containing contents of said eggs from the shells and Drying said separated antibody-containing contents of said eggs, said dried entire contents of said eggs when administered to the food animal inhibiting the adherence of the colony-forming bacteria in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony-forming bacteria being assisted by the IgM and IgA immunoglobulin, **does not** reasonably provide enablement for a method for the production of *any* microbial adherence inhibitor for administration to food animal or any living being as set forth in claims 1, 3, and 5-38. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient

to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a method of making microbial adherence inhibitor in the form of chicken egg antibody IgY that specifically bind to colony forming bacteria selected from the group consisting of *P. anaerobius*, *C. sticklandii*, *C. aminophilum*, *E coli serogroup 0157*. The microbial adherence inhibitor is produced by the method of growing said bacteria under specific condition to stimulate the expression of adherin or somatic antigen on the bacteria (pages 12-17), inoculating female chicken with the specific bacterial lysate or supernatant from bacteria such as *P. anaerobius*, *C. sticklandii*, *C. aminophilum*, and *E coli* serogroup *0157*, harvesting the eggs (page 20), whole egg containing the IgY in the yolk and IgM and IgA in the albumin is mixed, pasteurized, and store until dried or sprayed onto carriers such as pelleted soybean hulls as feed additive (page 22-23) prior to mixing with feed to feed animal to inhibit the adherence of said specific immunogen in the intestinal tracts of the animal and thereby promote the growth of the animal.

The specification does not teach how to make much less how to use any microbial adherence inhibitor in the form of egg antibody that binds to *any* undisclosed colony-forming immunogen because "immunogen" could be any antigen, any adherin or protein from bacteria, virus, or parasite. However, the peptide or protein antigen without the specific amino acid sequence has no structure. Further, there is inadequate guidance as to which undisclosed colony forming immunogen such as bacteria, parasite, or virus that when colonized the rumen or intestinal tracts of which animal would cause food wasting and reduce the growth of the animal. Until the colony-forming immunogen such as adherin on bacteria, virus, or parasite has been identified, it is unpredictable which immunogen used to inoculate female bird would produce microbial adherence inhibitor in the form of egg antibody that binds specifically to all colony-forming immunogen, in turn, useful for inhibiting the adherence of said immunogen in the rumen and intestinal tracts of all food animals.

Stryer *et al*, of record, teach that a protein (immunogen) is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages). Kuby *et al*, of record, teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment

derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide.

Abaza *et al*, of record, teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular).

Given the unlimited number of undisclosed colony-forming immunogen, it is unpredictable which undisclosed colony-forming immunogen would colonize the rumen or intestinal tracts and wasting dietary protein in which food animal. Further, there is no *in vivo* working example demonstrating that any of the microbial adherence inhibitor in the claimed method is effective for promoting the growth of all food animals by decreasing the waste of dietary protein. Given the unlimited number of microbial adherence inhibitor, there is insufficient guidance as to the binding specificity of the immunoglobulin, in turn, it would be useful for inhibiting the colony-forming immunogen to adhere to the rumen or intestinal tracts of all animals, let alone promoting the growth of all food animal by decreasing the waste of dietary protein.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Claim Rejections - 35 USC § 112 written description

Claims 1, 3, and 5-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of a method for the production of *any* microbial adherence inhibitor for administration to food animal or any living

being as set forth in claims 1, 3, and 5-38 to inhibit the ability of the protein-wasting immunogen to adhere to the rumen or intestinal tracts of the animals.

The specification discloses only a method of making microbial adherence inhibitor in the form of chicken egg antibody IgY that specifically bind to colony forming bacteria selected from the group consisting of *P. anaerobius, C. sticklandii, C. aminophilum, E coli serogroup 0157.* The microbial adherence inhibitor is produced by the method of growing said bacteria under specific condition to stimulate the expression of adherin or somatic antigen on the bacteria (pages 12-17), inoculating female chicken with the specific bacterial lysate or supernatant from bacteria such as *P. anaerobius, C. sticklandii, C. aminophilum,* and *E coli* serogroup *0157,* harvesting the eggs (page 20), whole egg containing the IgY in the yolk and IgM and IgA in the albumin is mixed, pasteurized, and store until dried or sprayed onto carriers such as pelleted soybean hulls as feed additive (page 22-23) prior to mixing with feed to feed animal to inhibit the adherence of said specific immunogen in the intestinal tracts of the animal and thereby promote the growth of the animal.

Other the specific colony-forming bacteria *P. anaerobius, C. sticklandii, C. aminophilium, E coli, Listeria, Salmonella* for a method of producing microbial adherence inhibitor in the form of IgY that binds specifically to said colony-forming bacteria to inhibit the adherence of said bacteria in the rumen or digestive track of food animal, there is inadequate written description about the colony-forming immunogen because "immunogen" without the specific amino acid sequence, or biochemical properties has no structure. Further, there is inadequate written description about which undisclosed colony forming immunogen such as bacteria, parasite, and virus that when colonized the rumen or intestinal tracts of which host would cause food wasting and reduce the growth of the animal. Until the "colony-forming immunogen" has been identified, the method of producing the microbial adherence inhibitor in form of egg antibody that binds to all undisclosed colony-forming immunogen cannot be made. Given the infinite number of undisclosed colony-forming immunogen, the method of producing said undisclosed colony forming immunogen has not been adequately described, and the binding specificity of microbial adherence inhibitor in the form of IgY including IgA and IgM is also not adequately described.

Since the specification discloses only a microbial inhibitor produced by growing bacteria under specific condition to stimulate the expression of adherin or somatic antigen on the bacteria, and then inoculating the hen with the bacterial lysate or supernatant from bacteria selected from

the group consisting of *P. anaerobius*, *C. sticklandii*, *C. aminophilum*, *E coli* serogroup 0157: H7, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the claimed method of producing a genus of colony-forming immunogens that inhibit the adherence of a colony forming immunogen in the digestive track of *all* living being. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398. University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 103

1. Claims 1, 3, 5, 8, 11, 14, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,080,895 (Tokoro et al, of record, Jan 1992; PTO 1449) or Yokoyama *et al* (Infection and Immunity 60(3): 998-1007, March 1992; PTO 892) each in view of Kaspers *et al* (Zentralbl Veterinarmed A 43(4): 225-31, June 1996; PTO 892), US Pat No 5,741,489 (Pimentel et al, of record, April 1998; PTO 1449), Krause *et al* (of record, Appl Environ Microbiol 62(3): 815-21; 1996, PTO 892), and Trinchieri *et al* (Urol Res 18(5): 305-8, 1990; PTO 892).

The '895 patent (Tokoro) teaches method of producing a microbial adherence inhibitor such as a yolk antibody that inhibits the targeted colony-forming bacteria (immunogen) such as *E coli* from adhering to the intestinal track of a living being such as livestock since the reference antibody is able to prevent diarrhea that results in wasting of dietary protein. The reference microbial adherence inhibitor is produced by inoculating an egg laying hen in their egg laying age with the reference immunogen such as bacterium *E coli* (See column 5, lines 29-30, in particular), allowing a period of time such as a few weeks after inoculation sufficient to permit the production of bird antibody that binds to the targeted immunogen such as *E coli* (See column 5, lines 47-60, column 6, 10-18, in particular), harvesting the egg laid by the hen (See column 6, line 1, in particular), separating the yolk and albumen (the entire content of the egg) (See column 6, lines 19-20, in particular), drying the separated egg antibody by spray drying or lyophilizing to form powder product (See column 6, line 24-25, in particular). The reference microbial adherence inhibitor such as dried egg antibody is used as an additive to food for animal or as a solution such as milk to livestock to prevent adherence of the targeted immunogen in the intestinal tract of the

animal (See column 9, line 42-46, column 10, line 30, column 5 lines 29 bridging column 6, lines 1-49, column 9, lines 43-57, column 10, line 29-31, in particular). The '895 patent further teaches various microbial adherence inhibitors such as egg antibodies produced by the method of inoculating the female bird with immunogens such as K88, K99 and 987P from *E coli* of interest; egg antibody is particularly advantageous due the fact that the procedure is simple, efficient and inexpensive (See column 9, line 43-47; column 3, line 19-27).

Yokoyama *et al* teach a method of producing a microbial adherence inhibitor such as IgY for administration to food animal such as piglets to inhibit the adherence of a targeted colony forming immunogen such as *E coli* in the intestinal tracts of the reference animal (See abstract, in particular). The reference method comprises inoculating the hen in or about to reach their egg laying age with the reference colony forming immunogen such as *E coli* (See page 999, Immunization with fimbrial vaccine, in particular), harvesting the eggs lay by the chickens and separating the IgY from the yolk (See page 999, column 2, Separation of antibodies from chicken egg yolk, in particular), drying the separated IgY (See page 1000, column 2, Production of antibody powders by spray drying, in particular) and when administering yolk antibodies to the living being such as neonatal piglets, the yolk antibodies inhibit the adherence of the colony forming immunogen E coli in the digestive tract.

The claimed invention in claims 1, and 5 differs from the teachings of the references only in that the method wherein the entire contents of the harvested eggs which include IgY in the yolks, and IgM and IgA in the albumin of the eggs are dried instead of separating the IgY from the yolk.

The claimed invention in claim 3 differs from the teachings of the references only in that the method wherein the colony-forming immunogen is selected from the class consisting of *P. anaerobius*, *C. sticklandii*, and *C. aminophilium*.

The claimed invention in claim 8 differs from the teachings of the references only in that the method wherein the entire contents of the harvested eggs which include IgY in the yolks, and IgM and IgA in the albumin of the eggs are dried and the microbial adherence inhibitor wherein the colony-forming immunogen is *P. anaerobius*.

The claimed invention in claim 11 differs from the teachings of the references only in that the method wherein the entire contents of the harvested eggs which include IgY in the yolks, and IgM and IgA in the albumin of the eggs are dried and the microbial adherence inhibitor wherein the colony-forming immunogen is *C. sticklandii*.

The claimed invention in claim 14 differs from the teachings of the reference only in that the method wherein the entire contents of the harvested eggs which include IgY in the yolks, and IgM and IgA in the albumin of the eggs are dried and the microbial adherence inhibitor wherein the colony-forming immunogen is *C. aminophilium.*

Kaspers *et al* teach IgG (IgY) is primary immunoglobulin isotype found in the egg yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular).

The '489 patent (Pimentel) teaches the use of whole egg (albumin and yolk) antibody which include IgY from the yolk and IgM and IgA from the albumin as evident by the teachings of Kaspers *et al* where the antibody can be dried and/or mixed with feed without first isolating the antibody from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular). The '489 patent teaches that antibodies have been reported to be more resistant to degradation by gastric acidity when are contained in the spay-dried whole egg (the entire contents) than mere purified sprayed-dried antibodies, i.e. IgY fraction (see column 2, lines 35-39, in particular). The '489 patent further teaches egg yolk antibodies that bind specifically to *E coli, Samonella* and other type of bacteria when administered to animal to prevent the bacteria in the gastro-intestinal tract from attaching to the intestinal wall and thereby decreasing the bacterial numbers by prventing bacterial multiplications (see col. 1, line 29-49, in particular).

Krause *et al* teach the colony-forming immunogens that are responsible for robbing cattle of nutrients are *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* (See entire document, page 820, col. 1, in particular). Krause *et al* further teach adding antibiotic such as monensin as a ruminant feed additive decreases ammonia accumulation in the rumen of cattle and inhibits the growth of monesin-sensitive obligate amino acid-fermenting bacteria such as *P. anaerobius* and *C. sticklandii* but not the number of *C. aminophilium* in livestock (see abstract, in particular).

Trinchieri *et al* teach that the attachment of *E coli* to human uroepithelial cells is inhibited by high level of the IgA (Abstract, in particular).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to substitute the immunogen such as the *E coli* as taught by the '895 patent (Tokoro) or Yokoyama et al for the *Peptostreptococcus anaerobius, Closteridium sticklandii, and/or Clostridium aminophilium* that are responsible for ruminal amino acid degradation in cattle as taught by Krause *et al* for a method of producing egg antibody such as IgY in the yolk as taught by the '895 patent (Tokoro) and Yokoyama et al and IgM and IgA in the albumin as taught

by Kasper et al. It would have been obvious to one ordinary skill in the art at the time the invention was made to dry the separated entire contents whole egg (white and yolk) antibody without first isolating the antibodies from the yolk as taught by the '489 patent (Pimentel) since (IgY) is primary the immunoglobulin isotype from the egg yolk while IgM and IgA are mainly found in the albumin as taught by Kaspers *et al* since egg antiobyd such as IgA can inhibit the attachment of bacteria to cell as taught by Trinchieri *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '489 patent (Pimentel) teaches that antibodies form the spay-dried whole egg are more resistant to degradation by gastric acidity than the purified (IgY yolk fraction) sprayed-dried antibodies (see column 2, lines 35-39, in particular). Kaspers *et al* teach IgG (IgY) is primary found in the yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular). Yokoyama et al teach when administered yolk antibodies to *E coli* to the living being such as neonatal piglets, the yolk antibodies inhibit the adherence of the colony forming immunogen E coli in the digest tract. Trinchieri et al teach that the attachment of *E coli* to human uroepithelial cells is inhibited by high level of the IgA (Abstract, in particular). Krause *et al* teach that bacteria such as *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* are responsible for nutrition depletion and the growth of livestock such as cattle (See entire document). Although monensin as a ruminant feed additive can decrease only the number of *P. anaerobius* and *C. sticklandii*, monesin does not decrease the number of *C. aminophilium* in livestock. It is within the purview of one ordinary skill in the pharmaceutical art to dry any antibody in the form of powder or dry antibody directly onto a carrier prior to administering to livestock as feed additive as taught by the '489 patent (Pimentel), Yokoyama *et al and* The '895 patent (Tokoro). The use of whole egg without separation as taught by the '489 patent (Pimentel) inherently includes the IgY in the yolk and the IgM and IgA in the albumin as taught by Kaspers *et al.*

2. Claims 5, 20, 23 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,080,895 (Tokoro et al, of record, Jan 1992; PTO 1449) or Yokoyama *et al* (Infection and Immunity 60(3): 998-1007, March 1992; PTO 892) each in view of Kaspers *et al* (Zentralbl Veterinarmed A 43(4): 225-31, June 1996; PTO 892), US Pat No 5,741,489 (Pimentel et al, of

record, April 1998; PTO 1449), Krause *et al* (of record, Appl Environ Microbiol 62(3): 815-21; 1996, PTO 892), and Trinchieri *et al* (Urol Res 18(5): 305-8, 1990; PTO 892) as applied to claims 1, 3, 5, 8, 11, 14, and 17 mentioned above and further in view of US Pat No 4,748,018 (Stolle et al, of record, May 31, 1988; PTO 1449), and Sugita-Konishi *et al* (of record, Biosci Biotechnol Biochem 60(5): 886-8, May 1996; PTO 892).

The combined teachings of the '895 patent (Tokoro), Yokoyama et al, Kaspers et al, the '489 (Pimentel), Krause *et al,* and Trinchieri *et al* have been discussed supra.

The claimed invention in claims 5, 20, 23 and 23 differs from the combined teachings of the references only in that the method wherein the colony-forming immunogen is *Listeria, Salmonella* or *Campylobacter.*

The '018 patent *et al* teach colony-forming immunogens such as *Listeria, Salmonella and Campylobacter* are responsible for various conditions such as salmonellitis in mammalian species and IgY antibody is useful for passive immunization. The '018 patent teaches a method of making IgY antibody to colony forming immunogen or combination of immunogen (antigen) such as *E coli, Listeria, Salmonella* and *Campylobacter* (See column 5, lines 1-30, column 6, line 22-25, in particular). The reference antibody is produced by inoculating an egg laying female birds such as the hen in their egg laying age with the reference immunogen or immunogens such as bacterium as *Listeria, Salmonella* and/or *Campylobacter*, wherein the reference immunogens are colony-forming bacteria that are known to cause food borne illness in humans by decreasing an animal's ability to absorb nutrient, allowing a period of time sufficient to permit the production of bird antibody that binds to the targeted immunogens, collecting the egg laid by the hen, purifying the reference antibody and lyophilizing or drying the separated egg antibody (See column 9, lines 17 bridging column 10, lines 1-29, in particular). The '018 patent teaches that the avian antibody is useful for a method of passive immunity (See abstract, in particular).

Sugita-Konishi *et al* teach a microbial adherence inhibitor such as IgY antibody obtained from hens immunized with a mixture of bacteria such as *Salamonella* that is responsible for salmonella enteritidis, the reference IgY microbial adherence inhibitor inhibits the adhesion of *Salamonella* to human intestinal cells (Caco 2) in culture (See abstract, and Materials and Methods, in particular).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to substitute the immunogen such as the *E coli* as taught by the '895 patent or Yokoyama, the bacteria such as *Peptostreptococcus anaerobius, Closteridium sticklandii, and*

Clostridium aminophilium as taught by Krause *et al* for the immunogen such as *Listeria, Salmonella* and/or *Campylobacter* as taught by the '018 patent or the *Salamonella* as taught by Sugita-Konishi *et al* for a method of producing a microbial adherence inhibitor such as immunoglobulins from whole egg that includes IgY from the yolk, and IgA and IgM antibodies in the albumin as taught by Kaspers *et al* to *Listeria, Salmonella* and/or *Campylobacter* as taught *by* the '018 patent, Sugita-Konishi *et al* or Yokoyama *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Sugita-Konishi *et al* teach that egg antibody to *Salamonella* inhibits the adhesion of *Salamonella* to human intestinal cells (Caco 2) in culture (See abstract, and Materials and Methods, in particular). The '018 patent teaches *E coli, Listeria, Salmonella* and *Campylobacter* are responsible for certain condition in mammals and that IgY antibody that binds specifically to colony forming immunogen or combination of immunogen (antigen) such as *E coli, Listeria, Salmonella* and *Campylobacter* (See column 5, lines 1-30, column 6, line 22-25, in particular) is useful for a method of passive immunity (See abstract, in particular). The '489 patent teaches that whole egg (white and yolk) antibody can be dried and mixed with feed without first isolating the antibodies from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular) and such antibodies have been reported to be more resistant to degradation by gastric acidity when are contained in the spay-dried whole egg as compared to purified sprayed-dried antibodies (see column 2, lines 35-39, in particular). Kaspers *et al* teach IgG (IgY) is the primary immunoglobulin isotype from the egg yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular). It is within the purview of one ordinary skill in the pharmaceutical art to dry any antibody in the form of powder or dry antibody directly onto a carrier prior to administering to livestock as feed additive as taught by the '489 patent (Pimentel), Yokoyama *et al and* The '895 patent (Tokoro).

3. Claims 6, 7, 9-10, 12-13, 15-16, 18-19, and 29-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,080,895 (Tokoro et al, of record, Jan 1992; PTO 1449) or Yokoyama *et al* (of record, Infection and Immunity 60(3): 998-1007, March 1992; PTO 892) each in view of Kaspers *et al* (of record, Zentralbl Veterinarmed A 43(4): 225-31, June 1996; PTO 892), US Pat No 5,741,489 (Pimentel et al, of record, April 1998; PTO 1449), Krause *et al* (of record, Appl Environ Microbiol 62(3): 815-21; 1996, PTO 892), and Trinchieri *et al* (Urol

Res 18(5): 305-8, 1990; PTO 892) as applied to claims 1, 3, 5, 8, 11, 14, and 17 mentioned above and further in view of US Pat 6,086,878 (Adalsteinsson et al, of record, Jul 2000, PTO 892) and US Pat No. 4,166,867 (of record, Sept 1979, PTO 892).

The combined teachings of the '895 patent (Tokoro), Yokoyama et al, Kaspers et al, the '489 (Pimentel), Krause *et al,* and Trinchieri *et al* have been discussed supra.

The claimed invention in claims 6, and 29 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins.

The claimed invention in claim 7, 9, 12, 15, 18, differs from the combined teachings of the references only in that the method including a dry carrier material, said drying the separated entire contents of said eggs is achieved by coating the dry carrier material with the separated entire contents of said eggs.

The claimed invention in claims 10, 13, 16, 19, 30, 33, 35, 37 differs from the combined teachings of the references only in that the method includes a dry carrier material, wherein the dry carrier material is from a group of materials including soybean hulls, rice hulls, corn, cottonseed hulls, distilled dried grains and beet pulp.

The claimed invention in claims 31 differs from the combined teachings of the references only in that the method wherein the target forming immunogen is from the class consisting of *P anaerobius, C sticklandii, and C aminophilium.*

The claimed invention in claim 32 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins and wherein the immunogen is P antigen from *P anaerobius*.

The claimed invention in claim 33 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins and wherein the immunogen is CS antigen from *C sticklanddi.*

The claimed invention in claim 36 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins and wherein the immunogen is CA antigen from *C aminiphilium.*

The claimed invention in claim 38 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins and wherein the immunogen is *E coli.*

The '878 patent (Adlasteinsson) teaches hyperimmunized spray-dried egg powder can be mixed with food animal feed rations or sprayed to coat directly onto carrier such as food pellets to maintaining sufficient antibody titers (See column 9, lines 37-46).

The '867 patent (Betz) teaches high performance palatable horse feed carrier such as soybean hulls, rice hulls cottonseed hulls provides the fibrous material and cereal grain such as corn and distilled dried grains provides the carbonaceous materials along with nutritional supplement (See column 3, lines 24-26, column 3, lines 10-18, claims of '867, in particular) while beet pulp provides high energy values (See column 2, line 12-13, in particular). The '867 patent teaches soybean hulls, rice hulls and cottonseed hulls provide the fibrous material as animal feed

in order to provide adequate structural strength or integrity to the final feed pellets and also to effect stool normality (See column 3, lines 14-16, in particular).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made by coating the dry feed carrier material such as soybean hulls, rice hulls and cottonseed hulls as taught by the '878 patent (Adlasteinsson) and/or the '867 patent (Betz) with the immunoglobulins from the entire contents of said eggs to *E coli, Peptostreptococcus anaerobius, Closteridium sticklandii,* or *Clostridium aminophilium* as taught by the '895 patent (Tokoro), Yokoyama et al, Kaspers et al, the '489 patent (Pimentel), Krause *et al,* and Trinchieri *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated with an expectation of success to mix antibody with food animal feed rations because the '878 patent (Adalsteinsson) teaches that hyperimmunized spray-dried egg can be mixed with food animal feed rations or sprayed to coat directly onto carrier such as food pellets to maintain antibody titers (See column 9, lines 37-46). The '867 patent (Betz) teaches soybean hulls, rice hulls and cottonseed hulls provide the fibrous material as animal feed in order to provide adequate structural strength or integrity to the final feed pellets and also to effect stool normality (See column 3, lines 14-16, in particular). The recitation of coating said dry feed carrier material with the separated contents of the harvested eggs without spray dried is an obvious variation of references teachings since the '489 patent (Pimentel) teach egg antibody from the whole egg (white and yolk) (without first isolating the antibodies) (see col. 2, line 7-8, in particular) can be mixed with carrier such as fine ground corn and then mixed with one metric ton feed (see col. 5, line 1-2, in particular). The '489 patent (Pimentel) further teaches that antibody activity is unaffected when eggs are spray dried (see col. 5, line 22-23, in particular). Further, the step of coating dry feed carrier material with the separate entire content of the eggs in the claimed method does not affect the production of microbial adherence inhibitor (IgY, IgM and IgA) antibodies. None of the rejected claims are drawn to a method of producing feed additive coated with the specific antibody. Trinchieri *et al* teach IgA to *E coli* could inhibit the attachment of *E coli* to human uroepithelial cells (Abstract, in particular). The '895 patent (Tokoro) teaches egg antibody is useful as an additive to food for animal or as a solution such as milk to livestock to prevent adherence of the targeted immunogen in the intestinal tract of the animal (See column 9, line 42-46, column 10, line 30, column 5 lines 29 bridging column 6, lines 1-49, column 9, lines 43-57, column 10, line 29-31, in particular).

Yokoyama *et al* teach administering IgY that binds specifically to immunogen such as *E coli* to food animal such as piglets would inhibit the adherence of a targeted colony forming immunogen such as *E coli* in the intestinal tracts of the reference animal (See abstract, in particular).

4. Claims 20-28 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,080,895 (Tokoro et al, of record, Jan 1992; PTO 1449) or Yokoyama *et al* (of record, Infection and Immunity 60(3): 998-1007, March 1992; PTO 892) each in view of Kaspers *et al* (of record, Zentralbl Veterinarmed A 43(4): 225-31, June 1996; PTO 892), US Pat No 5,741,489 (Pimentel et al, of record, April 1998; PTO 1449), Trinchieri *et al* (of record, Urol Res 18(5): 305-8, 1990; PTO 892), US Pat 6,086,878 (Adalsteinsson et al, of record, Jul 2000, PTO 892) and US Pat No. 4,166,867 (Betz et al, of record, Sept 1979, PTO 892), US Pat No 4,748,018 (Stolle et al, of record, May 31, 1988; PTO 1449), and Sugita-Konishi *et al* (of record, Biosci Biotechnol Biochem 60(5): 886-8, May 1996; PTO 892).

The '895 patent (Tokoro) teaches method of producing a microbial adherence inhibitor such as a yolk antibody that inhibits the targeted colony-forming bacteria (immunogen) such as *E coli* from adhering to the intestinal track of a living being such as livestock since the reference antibody is able to prevent diarrhea that results in wasting of dietary protein. The reference microbial adherence inhibitor is produced by inoculating an egg laying hen in their egg laying age with the reference immunogen such as bacterium *E coli* (See column 5, lines 29-30, in particular), allowing a period of time such as a few weeks after inoculation sufficient to permit the production of bird antibody that binds to the targeted immunogen such as *E coli* (See column 5, lines 47-60, column 6, 10-18, in particular), harvesting the egg laid by the hen (See column 6, line 1, in particular), separating the yolk and albumen (the entire content of the egg) (See column 6, lines 19-20, in particular), drying the separated egg antibody by spray drying or lyophilizing to form powder product (See column 6, line 24-25, in particular). The reference microbial adherence inhibitor such as dried egg antibody is used as an additive to food for animal or as a solution such as milk to livestock to prevent adherence of the targeted immunogen in the intestinal tract of the animal (See column 9, line 42-46, column 10, line 30, column 5 lines 29 bridging column 6, lines 1-49, column 9, lines 43-57, column 10, line 29-31, in particular). The '895 patent further teaches various microbial adherence inhibitors such as egg antibodies produced by the method of inoculating the female bird with immunogens such as K88, K99 and 987P from *E coli* of interest;

egg antibody is particularly advantageous due the fact that the procedure is simple, efficient and inexpensive (See column 9, line 43-47; column 3, line 19-27).

Yokoyama *et al* teach a method of producing a microbial adherence inhibitor such as IgY for administration to food animal such as piglets to inhibit the adherence of a targeted colony forming immunogen such as *E coli* in the intestinal tracts of the reference animal (See abstract, in particular). The reference method comprises inoculating the hen in or about to reach their egg laying age with the reference colony forming immunogen such as *E coli* (See page 999, Immunization with fimbrial vaccine, in particular), harvesting the eggs lay by the chickens and separating the IgY from the yolk (See page 999, column 2, Separation of antibodies from chicken egg yolk, in particular), drying the separated IgY (See page 1000, column 2, Production of antibody powders by spray drying, in particular) and when administering yolk antibodies to the living being such as neonatal piglets, the yolk antibodies inhibit the adherence of the colony forming immunogen *E coli* in the digestive tract.

The claimed invention in claim 21, 24, and 27 differs from the combined teachings of the references only in that the method including a dry carrier material, said drying the separated entire contents of said eggs is achieved by coating the dry carrier material with the separated entire contents of said eggs.

The claimed invention in claims 22, 25, and 28 differs from the combined teachings of the references only in that the method including a dry carrier material, said drying the separated entire contents of said eggs is achieved by coating the dry carrier material with the separated entire contents of said eggs wherein the dry carrier material is from a group of materials including soybean hulls, rice hulls, corn, cottonseed hulls, distilled dried grains and beet pulp.

The claimed invention in claim 38 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins and wherein the immunogen is *Listeria, Salmonella* and *Campylobacter.*

Kaspers *et al* teach IgG (IgY) is primary immunoglobulin isotype from the egg yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular).

The '489 patent (Pimentel) teaches the use of whole egg (albumin and yolk) antibody which include IgY from the yolk and IgM and IgA from the albumin as evident by the teachings of Kaspers *et al* where the antibody can be dried and/or mixed with feed without first isolating the antibody from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular). The '489 patent teaches that antibodies have been reported to be more resistant to degradation by gastric acidity when are contained in the spay-dried whole egg (the entire contents) than mere purified sprayed-dried antibodies, i.e. IgY fraction (see column 2, lines 35-39, in particular). The '489 patent further teaches egg yolk antibodies that bind specifically to *E coli, Samonella* and other type of bacteria when administered to animal to prevent the bacteria in the gastro-intestinal tract from attaching to the intestinal wall and thereby decreasing the bacterial numbers by prventing bacterial multiplications (see col. 1, line 29-49, in particular).

Trinchieri *et al* teach that the attachment of *E coli* to human uroepithelial cells is inhibited by high level of the IgA (Abstract, in particular).

The '878 patent (Adlasteinsson) teaches hyperimmunized spray-dried egg powder can be mixed with food animal feed rations or sprayed to coat directly onto carrier such as food pellets to maintaining sufficient antibody titers (See column 9, lines 37-46).

The '867 patent (Betz) teaches high performance palatable horse feed carrier such as soybean hulls, rice hulls cottonseed hulls provides the fibrous material and cereal grain such as corn and distilled dried grains provides the carbonaceous materials along with nutritional supplement (See column 3, lines 24-26, column 3, lines 10-18, claims of '867, in particular) while beet pulp provides high energy values (See column 2, line 12-13, in particular). The '867 patent teaches soybean hulls, rice hulls and cottonseed hulls provide the fibrous material as animal feed in order to provide adequate structural strength or integrity to the final feed pellets and also to effect stool normality (See column 3, lines 14-16, in particular).

The '018 patent (Stolle) teaches colony-forming immunogens such as *Listeria, Salmonella and Campylobacter* are responsible for various conditions such as salmonellitis in mammalian species and IgY antibody is useful for passive immunization. The '018 patent (Stolle) teaches a method of making IgY antibody to colony forming immunogen or combination of immunogen (antigen) such as *E coli, Listeria, Salmonella* and *Campylobacter* (See column 5, lines 1-30, column 6, line 22-25, in particular). The reference antibody is produced by inoculating an egg laying female birds such as the hen in their egg laying age with the reference immunogen or immunogens such as bacterium as *Listeria, Salmonella* and/or *Campylobacter*,

wherein the reference immunogens are colony-forming bacteria that are known to cause food borne illness in humans by decreasing an animal's ability to absorb nutrient, allowing a period of time sufficient to permit the production of bird antibody that binds to the targeted immunogens, collecting the egg laid by the hen, purifying the reference antibody and lyophilizing or drying the separated egg antibody (See column 9, lines 17 bridging column 10, lines 1-29, in particular). The '018 patent teaches that the avian antibody is useful for a method of passive immunity (See abstract, in particular).

Sugita-Konishi *et al* teach a microbial adherence inhibitor such as IgY antibody obtained from hens immunized with a mixture of bacteria such as *Salamonella* that is responsible for salmonella enteritidis, the reference IgY microbial adherence inhibitor inhibits the adhesion of *Salamonella* to human intestinal cells (Caco 2) in culture (See abstract, and Materials and Methods, in particular).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to dry antibody as taught by the '878 patent (Adalsteinsson) by coating the dry feed as carrier material such as soybean hulls, rice hulls and cottonseed hulls as taught by the '867 patent (Betz) with the immunoglobulins from the entire contents of said eggs as taught by the '489 patent (Pimentel) that contains IgY from the yolk and IgA and IgM as taught by Kaspers *et al* to immunogen such as *E coli* as taught by the '895 patent (Tokoro) or Yokoyama et al, *Listeria, Salmonella* and *Campylobacter* as taught by the '018 patent (Stolle). From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated with an expectation of success to mix antibody with food animal feed rations because the '878 patent (Adalsteinsson) teaches that hyperimmunized spray-dried egg can be mixed with food animal feed rations or sprayed to coat directly onto carrier such as food pellets to maintain antibody titers (See column 9, lines 37-46). The '867 patent (Betz) teaches soybean hulls, rice hulls and cottonseed hulls provide the fibrous material as animal feed in order to provide adequate structural strength or integrity to the final feed pellets and also to effect stool normality (See column 3, lines 14-16, in particular). The recitation of coating said dry feed carrier material with the separated contents of the harvested eggs without spray dried is an obvious variation of references teachings since the '489 patent (Pimentel) teach egg antibody from the whole egg (white and yolk) (without first isolating the antibodies) (see col. 2, line 7-8, in particular) can be mixed with carrier such as fine

ground corn and then mixed with one metric ton feed (see col. 5, line 1-2, in particular). The '489 patent (Pimentel) further teaches that antibody activity is unaffected when eggs are spray dried (see col. 5, line 22-23, in particular). Further, the method of coating dry food carrier is an obvious variation of the teachings of the'489 patent (Pimentel) since whole egg (white and yolk) antibody can be dried and/or mixed with feed without first isolating the antibodies from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular). The '489 patent further teaches that antibodies have been reported to be more resistant to degradation by gastric acidity when are contained in the spay-dried whole egg (the entire contents) than mere purified sprayed-dried antibodies, i.e. IgY fraction (see column 2, lines 35-39, in particular). Trinchieri *et al* teach IgA to *E coli* could inhibit the attachment of *E coli* to human uroepithelial cells (Abstract, in particular). The '895 patent (Tokoro) teaches egg antibody is useful as an additive to food for animal or as a solution such as milk to livestock to prevent adherence of the targeted immunogen in the intestinal tract of the animal (See column 9, line 42-46, column 10, line 30, column 5 lines 29 bridging column 6, lines 1-49, column 9, lines 43-57, column 10, line 29-31, in particular). Yokoyama *et al* teach administering IgY that binds specifically to immunogen such as *E coli* to food animal such as piglets would inhibit the adherence of a targeted colony forming immunogen such as *E coli* in the intestinal tracts of the reference animal (See abstract, in particular).

(11) Response to Argument

Claim Rejections - 35 USC § 112 first enablement

At page 10-11 of the Brief, Appellants submit that the specification clearly discloses Appellants' method for the production of a microbial adherence inhibitor promoting the growth of living beings including food animals by decreasing the waste of dietary protein caused by the presence of a protein-wasting immunogen in the rumen or intestinal tracts of food animals and living beings. The Examiner has construed the requirements of 35 USC 1 12 to include any person skilled in the art to make and use the invention commensurate in scope with the claims. Office action 2/13/2004, page 2, lines 24-26. This is not the requirement of 35 USC 112 ¶1. It is the specification, according to 35 USC 112 ¶1, that contains the written description to enable a person skilled in the art to make and use the same. The specification describes the methods of Selection of Egg laying avian hens, pages 12-13; Preparation of Stock Culture, page 12; Preparation of H antigens for Immunogens pages 13-14; Preparation of O antigens for immunogens, pages 14-15; Preparation of A antigen for immunogen, pages 15-16; Preparation of P antigen for immunogen, pages 16-17; Preparation of CA antigen for immunogen, pages 17-18;

Analysis of individual eggs and serum over time, page 19; Immunization of chickens with immunogens, page 20-22; and Feeding of Cattle, pages 27-28. The specification contains a detailed description and best mode of Appellants' process of promoting the growth of food animals, such as cattle, by decreasing the waste of dietary protein caused by the presence of a protein-wasting immunogen in the rumen of intestinal tracts of the animals by inhibiting the ability of the immunogen to adhere to the rumen or intestinal tracts of the animals to reduce the ability of the immunogen to multiply. This description enables a person skilled in the art to make and use the subject method for the production of a microbial adherence inhibitor.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. Appellants' argument seems to go more toward description than enablement. The examiner's rejection is based on the scope of enablement, not lack of written description.

The claims encompasses a method for the production of all microbial adherence inhibitor such as avian antibody (IgY immunoglobulin) to any targeted colony-forming immunogen by inoculating the female chickens with any targeted colony-forming immunogen and when administered to any food animals, the IgY immunoglobulin promotes the growth of all food animals by decreasing the waste of dietary protein and the binding of IgY immunoglobulins to the protein-wasting immunogen being assisted by the IgM and IgA immunoglobulins to inhibit the ability of the targeted colony-forming immunogen to adhere to the rumen or intestinal tracts of the animals.

The specification discloses only a method of making microbial adherence inhibitor in the form of chicken egg antibody IgY that specifically bind to colony forming bacteria selected from the group consisting of *P. anaerobius*, *C. sticklandii*, *C. aminophilum*, *E coli serogroup 0157*. The microbial adherence inhibitor is produced by the method of growing said bacteria under specific condition to stimulate the expression of adherin or somatic antigen on the bacteria (pages 12-17), inoculating female chicken with the specific bacterial lysate or supernatant from bacteria such as *P. anaerobius*, *C. sticklandii*, *C. aminophilum*, and *E coli* serogroup *0157*, harvesting the eggs (page 20), whole egg containing the IgY in the yolk and IgM and IgA in the albumin is mixed, pasteurized, and store until dried or sprayed onto carriers such as pelleted soybean hulls as feed additive (page 22-23) prior to mixing with feed to feed animal to inhibit the adherence of said specific immunogen in the intestinal tracts of the animal and thereby promote the growth of the animal.

The specification does not teach how to make all microbial adherence inhibitors such as IgY immunoglobulins that bind to all "colony-forming immunogen". There is inadequate guidance about the colony-forming immunogen because "colony-forming immunogen" could be any molecules or "adherins" or somatic antigens on the surface of any colonizing microorganisms such as bacteria, viruses and parasites, etc as disclosed on page 12, line 8-10. Without the specific amino acid sequence, or biochemical properties, the "colony-forming immunogen" has no structure. Even if the "colony-forming immunogen" is limited to *E coli*, the specification discloses certain antigens such as H antigen, O antigen, A antigen, and WC antigen on *E coli* must be cultured in a specific medium (see Example 3-5 on page 13-15 of the specification). There is insufficient guidance as to which condition medium to grow other undisclosed "colony-forming immunogen". There is insufficient guidance as to which undisclosed adherins or somatic antigens on all colony forming immunogen is responsible for adhering to the rumen or intestinal tracts of which host and which "colony forming immunogen" is the causative agent for wasting food in which host. Until the "colony-forming immunogen", inoculating female chickens with any targeted "colony-forming immunogen" would not produce immunoglobulins from egg that bind specifically to which adherin on the surface of any bacteria, any virus and any parasite that are responsible for wasting dietary protein in all host.

Stryer *et al*, of record, teach that a protein (immunogen) is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages). Kuby *et al*, of record, teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide.

Abaza *et al*, of record, teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the unlimited number of undisclosed colony-forming immunogen, it is unpredictable which undisclosed colony-forming immunogen would colonize the rumen or intestinal tracts and wasting dietary protein in which food animal. Further, there is no *in vivo* working example demonstrating that any of the microbial adherence inhibitor in the claimed method is effective for promoting the growth of all food animals by decreasing the

waste of dietary protein. Given the unlimited number of microbial adherence inhibitor, there is insufficient guidance as to the binding specificity of the immunoglobulin, in turn, it would be useful for inhibiting the colony-forming immunogen to adhere to the rumen or intestinal tracts of all animals, let alone promoting the growth of all food animal by decreasing the waste of dietary protein.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Claim Rejections - 35 USC § 112 first Written Description

At page 11 first full paragraph of the Brief, Appellants submit that the specification states that the IgY immunoglobulins very tightly bind to, coat, cover and obliterate adherins which attach themselves to their hosts. Page 12, lines 11-13. The particular language is the "binding of IgY immunogens to protein-wasting immunogens is being increased by the IgM and IgA immunoglobulins." This function is supported by the disclosure that hen layers the unique IgY types immunoglobulins in the yolk while depositing the chicken IgM and IgA immunoglobulins in the albumin. The albumin helps resistance to the whole egg preparations and helps protect the avian antibodies. Specification page 10, lines 4-5. The whole egg preparation includes the IgY immunoglobulins in the yolk and IgM and IgA immunoglobulins in the albumin. The term "helps" means aids, assists and encourages the protection of the avian antibodies. This language supports the increase in the finding of IgY immunogens to the protein-wasting immunogens as more IgY immunogens are available to bind to the protein-wasting immunogens.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. In contrast to Appellants' assertion that the "binding of IgY immunogens to protein-wasting immunogens is being *increased* by the IgM and IgA immunoglobulins", the specification on page 10, lines 2-4 discloses that "Once immunized the hen layers the unique IgY types

immunoglobulins in the yolk while depositing the common chicken IgM and IgA immunoglobulins in the albumin. The albumin helps resistance to the whole egg preparations and helps protect the avian antibodies." Neither the specification's description nor the exemplary embodiments provide any evidence that the binding of IgY immunoglobulins microbial adherence inhibitors to any protein wasting immunogens is being *increased* by the IgM and IgA immunoglobulins.

At paragraph bridging pages 11 and 12 of the Brief, Appellants submit that the albumin IgM and IgA immunoglobulins increase binding in the mucus tissue of the digestive tract of the antibody containing material thereby providing a longer sustaining effect of the antibody containing material. The IgM and IgA immunoglobulins have di-sulfide bonds that retain molecules together and provide larger antibody containing molecules. The larger antibody containing molecules are more effective in preventing adherence of the targeted immunogen in the digestive tract of the animal. Albumin is a protein that protects the activity of the IgY type immunoglobulins thereby increasing their active life in the intestinal tract. The result is the use of the antibody whole egg, yolk and albumin, mixed with animal feed or water substantially prevents adherence of the targeted immunogen in the digestive tract of the animal.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. In contrast to Appellants' assertion that the albumin IgM and IgA immunoglobulins increase binding in the mucus tissue of the digestive tract of the antibody containing material thereby providing a longer sustaining effect of the antibody containing material, neither the specification's description nor the exemplary embodiments provide any evidence that IgM and IgA immunoglobulins increase binding of IgY in the mucus tissue of the digestive tract of any animals. The di-sulfide bonds in the IgM and IgA immunoglobulins are irrelevant to the claimed method of production of a microbial adherence inhibitor.

At page 12 second paragraph of the Brief, Appellants assert that the specification provides a representative number of species of colony-forming protein-wasting immunogens to describe the genus identified by the terms target colony-forming immunogens. These immunogens are well known protein-wasting immunogens. The species of immunogens are identified as from a class consisting of: *P. anaerobius, C. sticklandii, C. aminophilium, E. coli, Listeria, Salmonella and Campylobacter.* This class is sufficient to identify a genus of like

immunogens to a person skilled in the art. One skilled in the art would be aware of the bacterial antigens noted by Stolle et al '018 in column 5, lines 5-35. Claims 1, 3, 5-38 particularly point out and distinctly claim the subject matter of Appellants' method for the production of a microbial adherence inhibitor as described in the specification.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive.

The claims encompasses a method for the production of all microbial adherence inhibitor such as avian antibody (IgY immunoglobulin) to all targeted colony-forming immunogen by inoculating the female chickens with any targeted colony-forming immunogen and when administered to any food animals, the IgY immunoglobulin promotes the growth of all food animals by decreasing the waste of dietary protein and the binding of IgY immunoglobulins to the protein-wasting immunogen being assisted by the IgM and IgA immunoglobulins to inhibit the ability of the targeted colony-forming immunogen to adhere to the rumen or intestinal tracts of the animals.

The specification discloses only a method of making microbial adherence inhibitor in the form of chicken egg antibody IgY that specifically bind to colony forming bacteria selected from the group consisting of *P. anaerobius*, *C. Sticklandii*, *C. aminophilum*, *E coli serogroup 0157.* The microbial adherence inhibitor is produced by the method of growing said bacteria under specific condition to stimulate the expression of adherenin or somatic antigen on the bacteria (pages 13-17), inoculating female chicken with the specific bacterial lysate or supernatant from bacteria such as *P. anaerobius*, *C. sticklandii*, *C. aminophilum*, and *E coli* serogroup *0157,* harvesting the eggs (page 20), whole egg containing the IgY in the yolk and IgM and IgA in the albumin is mixed, pasteurized, and store until dried or sprayed onto carriers such as pelleted soybean hulls as feed additive (page 22-23) prior to mixing with feed to feed animal to inhibit the adherence of said specific immunogen in the intestinal tracts of the animal and thereby promote the growth of the animal.

Other the specific colony-forming bacteria *P. anaerobius, C. sticklandii, C. aminophilium, E coli, Listeria, Salmonella* for a method of producing microbial adherence inhibitor in the form of IgY that binds specifically to said colony-forming bacteria to inhibit the adherence of said bacteria in the rumen or digestive track of food animal, there is inadequate written description about the colony-forming immunogen because "immunogen" without the specific amino acid sequence, or biochemical properties has no structure. Further, there is

inadequate written description about which undisclosed colony forming immunogen such as bacteria, parasite, and virus that when colonized the rumen or intestinal tracts of which host would cause food wasting and reduce the growth of the animal. Until the "colony-forming immunogen" has been identified, the method of producing the microbial adherence inhibitor in form of egg antibody that binds to all undisclosed colony-forming immunogen cannot be made. Given the infinite number of undisclosed colony-forming immunogen, the method of producing said undisclosed colony forming immunogen has not been adequately described, and the binding specificity of microbial adherence inhibitor in the form of IgY including IgA and IgM is also not adequately described.

Since the specification discloses only a microbial inhibitor produced by growing bacteria under specific condition to stimulate the expression of adherenin or somatic antigen on the bacteria, and then inoculating the hen with the bacterial lysate or supernatant from bacteria selected from the group consisting of *P. anaerobius*, *C. sticklandii*, *C. aminophilum*, *E coli* serogroup 0157: H7, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the claimed method of producing a genus of colony-forming immunogens that inhibit the adherence of a colony forming immunogen in the digestive track of *all* living being. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398. University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Claim Rejections - 35 USC § 103

Rejection of Claims 1, 3, 5, 8, 11, 14, and 17 under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,080,895 (Tokoro et al, of record, Jan 1992; PTO 1449) or Yokoyama *et al* (Infection and Immunity 60(3): 998-1007, March 1992; PTO 892) each in view of Kaspers *et al* (Zentralbl Veterinarmed A 43(4): 225-31, June 1996; PTO 892), US Pat No 5,741,489 (Pimentel et al, of record, April 1998; PTO 1449), Krause *et al* (of record, Appl Environ Microbiol 62(3): 815-21; 1996, PTO 892), and Trinchieri *et al* (Urol Res 18(5): 305-8, 1990; PTO 892).

At page 14-15 of the Brief, Appellants begin the argument by summarizing the invention of Claims 1 and 5, which define a method for the production of a microbial adherence inhibitor that inhibits the adherence of a targeted colony-forming immunogen in the intestinal tracts of living beings including animals. This is accomplished by using the entire contents of eggs having

the IgY immunoglobulins and IgM and IgA immunoglobulins to promote the growth of the animals by decreasing the waste of dietary protein caused by the presence of protein-wasting immunogens in the intestinal tracts of the animals. The IgY immunoglobulins bind to the protein-wasting immunogens which inhibits the ability of the protein-wasting immunogens to adhere to the intestinal tracts of the animals. The binding process is assisted and helped by the IgM and IgA immunoglobulins. Claim 3 depends upon Claim 1. Claim 3 further defines the targeted colony-forming immunogen as being from the class consisting of *P. anaerobius, C. sticklandii and C. aminophilium.* Claims 8, 11, 14 and 17 define a method for the production of a microbial adherence inhibitor for promoting growth of food animals by decreasing waste of dietary protein caused by protein-wasting immunogen. The entire contents of eggs having the IgY immunoglobulins and IgM and IgA immunoglobulins are administered to the animals to promote the growth of the animals by decreasing the waste of dietary protein caused by the presence of protein-wasting immunogens in the intestinal tracts of the animals. The IgY immunoglobulins bind to the protein-wasting immunogens which inhibits the ability of the protein-wasting immunogens to adhere to the intestinal tracks of the animals. The binding process is assisted and helped by the IgM and IgA immunoglobulins. The protein-wasting immunogens are identified as P antigen from *P. anaerobius, C. sticklandii and C. aminophilium* and *E. coli* antigen from *E. coli*. Appellants submit that Tokoro ('895 patent) teaches a method of inhibiting diarrhea in animals with bird antibody IgY using the yolks, the albumin and the yolks of the eggs. This method is related to the use of raw eggs by cattle herdpersons to treat scours (diarrhea in cattle caused by intestinal infection). The '895 patent (Tokoro) is directed to a specific antibody containing substance from eggs and method of production and use thereof for the prevention and treatment of colibacillosis and diarrhea in animals. There is no disclosure in Tokoro '895 of an IgY immunoglobulin that binds to a colony-forming immunogen. The antibody is used as nutrition supplement, and as an additive to food for animals. Tokoro '895 does not provides a teaching of a method promoting the growth of food animals by binding IgY immunoglobulins combined with IgM and IgA immunoglobulins to protein wasting immunogens, P antigen from *P. anaerobius*, CS antigen from *C. sticklandii*, and CA antigen from *C. aminophilium*, and *E. coli* antigen from *E. Coli*.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive for the following reasons.

First, it is noted that the "colony-forming immunogen" in claims 1 and 6 is any molecule or "adherins" or "somatic antigen" on any colonizing microorganism such as bacteria, virus and parasites as defined on page 12, lines 8-10 of the specification.

Second, it is noted that none of the rejected claims recite the specific molecule or adherins expressed on the particular colony-forming immunogen.

Third, none of the rejected claims recite the specific step of preparing the specific colony-forming immunogen.

Fourth, in response to appellants' arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Fifth, in contrast to appellants assertion that there is no disclosure in Tokoro ('895 patent) of an IgY immunoglobulin that binds to a colony-forming immunogen, the '895 patent (Tokoro) teaches method of producing a microbial adherence inhibitor such as a yolk antibody that inhibits the targeted colony-forming bacteria (immunogen) such as *E coli* from adhering to the intestinal track of a living being such as livestock since the reference antibody is able to prevent diarrhea that results in wasting of dietary protein. The reference microbial adherence inhibitor is produced by inoculating an egg laying hen in their egg laying age with the reference immunogen such as bacterium *E coli* (See column 5, lines 29-30, in particular), allowing a period of time such as a few weeks after inoculation sufficient to permit the production of bird antibody that binds to the targeted immunogen such as *E coli* (See column 5, lines 47-60, column 6, 10-18, in particular), harvesting the egg laid by the hen (See column 6, line 1, in particular), separating the yolk and albumen (the entire content of the egg) (See column 6, lines 19-20, in particular), drying the separated egg antibody by spray drying or lyophilizing to form powder product (See column 6, line 24-25, in particular). The reference microbial adherence inhibitor such as dried egg antibody is used as an additive to food for animal or as a solution such as milk to livestock to prevent adherence of the targeted immunogen in the intestinal tract of the animal (See column 9, line 42-46, column 10, line 30, column 5 lines 29 bridging column 6, lines 1-49, column 9, lines 43-57, column 10, line 29-31, in particular). The '895 patent further teaches various microbial adherence inhibitors such as egg antibodies produced by the method of inoculating the female bird with immunogens such as K88, K99 and 987P from *E coli* of interest; egg antibody is

particularly advantageous due the fact that the procedure is simple, efficient and inexpensive (See column 9, line 43-47; column 3, line 19-27).

Yokoyama *et al* teach a method of producing a microbial adherence inhibitor such as IgY for administration to food animal such as piglets to inhibit the adherence of a targeted colony forming immunogen such as *E coli* in the intestinal tracts of the reference animal (See abstract, in particular). The reference method comprises inoculating the hen in or about to reach their egg laying age with the reference colony forming immunogen such as *E coli* (See page 999, Immunization with fimbrial vaccine, in particular), harvesting the eggs lay by the chickens and separating the IgY from the yolk (See page 999, column 2, Separation of antibodies from chicken egg yolk, in particular), drying the separated IgY (See page 1000, column 2, Production of antibody powders by spray drying, in particular) and when administering yolk antibodies to the living being such as neonatal piglets, the yolk antibodies inhibit the adherence of the colony forming immunogen *E coli* in the digestive tract.

The claimed invention in claims 1, and 5 differs from the teachings of the references only in that the method wherein the entire contents of the harvested eggs which include IgY in the yolks, and IgM and IgA in the albumin of the eggs are dried instead of separating the IgY from the yolk.

The claimed invention in claim 3 differs from the teachings of the references only in that the method wherein the colony-forming immunogen is selected from the class consisting of *P. anaerobius*, *C. sticklandii*, and *C. aminophilium*.

The claimed invention in claim 8 differs from the teachings of the references only in that the method wherein the entire contents of the harvested eggs which include IgY in the yolks, and IgM and IgA in the albumin of the eggs are dried and the microbial adherence inhibitor wherein the colony-forming immunogen is *P. anaerobius*.

The claimed invention in claim 11 differs from the teachings of the references only in that the method wherein the entire contents of the harvested eggs which include IgY in the yolks, and IgM and IgA in the albumin of the eggs are dried and the microbial adherence inhibitor wherein the colony-forming immunogen is *C. sticklandii*.

The claimed invention in claim 14 differs from the teachings of the reference only in that the method wherein the entire contents of the harvested eggs which include IgY in the yolks, and IgM and IgA in the albumin of the eggs are dried and the microbial adherence inhibitor wherein the colony-forming immunogen is *C. aminophilium*.

Kaspers *et al* teach IgG (IgY) is primary immunoglobulin isotype found in the egg yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular).

The '489 patent (Pimentel) teaches the use of whole egg (albumin and yolk) antibody which include IgY from the yolk and IgM and IgA from the albumin as evident by the teachings of Kaspers *et al* where the antibody can be dried and/or mixed with feed without first isolating the antibody from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular). The '489 patent teaches that antibodies have been reported to be more resistant to degradation by gastric acidity when are contained in the spay-dried whole egg (the entire contents) than mere purified sprayed-dried antibodies, i.e. IgY fraction (see column 2, lines 35-39, in particular). The '489 patent further teaches egg yolk antibodies that bind specifically to *E coli, Samonella* and other type of bacteria when administered to animal to prevent the bacteria in the gastro-intestinal tract from attaching to the intestinal wall and thereby decreasing the bacterial numbers by prventing bacterial multiplications (see col. 1, line 29-49, in particular).

Krause *et al* teach the colony-forming immunogens that are responsible for robbing cattle of nutrients are *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* (See entire document, page 820, col. 1, in particular). Krause *et al* further teach adding antibiotic such as monensin as a ruminant feed additive decreases ammonia accumulation in the rumen of cattle and inhibits the growth of monesin-sensitive obligate amino acid-fermenting bacteria such as *P. anaerobius* and *C. sticklandii* but not the number of *C. aminophilium* in livestock (see abstract, in particular).

Trinchieri *et al* teach that the attachment of *E coli* to human uroepithelial cells is inhibited by high level of the IgA (Abstract, in particular).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to substitute the immunogen such as the *E coli* as taught by the '895 patent (Tokoro) or Yokoyama et al for the *Peptostreptococcus anaerobius, Closteridium sticklandii, and/or Clostridium aminophilium* that are responsible for ruminal amino acid degradation in cattle as taught by Krause *et al* for a method of producing egg antibody such as IgY in the yolk as taught by the '895 patent (Tokoro) and Yokoyama et al and IgM and IgA in the albumin as taught by Kasper et al. It would have been obvious to one ordinary skill in the art at the time the invention was made to dry the separated entire contents whole egg (white and yolk) antibody without first isolating the antibodies from the yolk as taught by the '489 patent (Pimentel) since (IgY) is primary the immunoglobulin isotype from the egg yolk while IgM and IgA are mainly

found in the albumin as taught by Kaspers *et al* since egg antiobyd such as IgA can inhibit the attachment of bacteria to cell as taught by Trinchieri *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '489 patent (Pimentel) teaches that antibodies form the spay-dried whole egg are more resistant to degradation by gastric acidity than the purified (IgY yolk fraction) sprayed-dried antibodies (see column 2, lines 35-39, in particular). Kaspers *et al* teach IgG (IgY) is primary found in the yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular). Yokoyama et al teach when administered yolk antibodies to *E coli* to the living being such as neonatal piglets, the yolk antibodies inhibit the adherence of the colony forming immunogen E coli in the digest tract. Trinchieri et al teach that the attachment of *E coli* to human uroepithelial cells is inhibited by high level of the IgA (Abstract, in particular). Krause *et al* teach that bacteria such as *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* are responsible for nutrition depletion and the growth of livestock such as cattle (See entire document). Although monensin as a ruminant feed additive can decrease only the number of *P. anaerobius* and *C. sticklandii*, monesin does not decrease the number of *C. aminophilium* in livestock. It is within the purview of one ordinary skill in the pharmaceutical art to dry any antibody in the form of powder or dry antibody directly onto a carrier prior to administering to livestock as feed additive as taught by the '489 patent (Pimentel), Yokoyama *et al and* The '895 patent (Tokoro). The use of whole egg without separation as taught by the '489 patent (Pimentel) inherently includes the IgY in the yolk and the IgM and IgA in the albumin as taught by Kaspers *et al.*

At page 15 second full paragraph of the Brief, Appellants argue that there is no disclosure in the Kaspers et al publication of IgY, IgM and IgA immunoglobulins whereby the IgY immunoglobulins bind to colony-forming or protein-wasting immunogens with the binding process being assisted by the IgM and IgA immunoglobulins thereby inhibiting the colony-forming or protein-wasting immunogens from adhering to the intestinal tracts of animals.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive for the following reasons. In response to appellants' arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871

(CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145. The '489 patent (Pimentel) teaches the use of whole egg (white and yolk) antibody can be dried and/or mixed with feed without first isolating the antibodies from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular). The '489 patent (Pimentel) further teaches that antibodies have been reported to be more resistant to degradation by gastric acidity when are contained in the spay-dried whole egg (the entire contents) than mere purified sprayed-dried antibodies, i.e. IgY fraction (see column 2, lines 35-39, in particular). Kaspers *et al* teach IgG (IgY) is primary immunoglobulin isotype found in egg yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular). The whole egg preparation as taught by the '489 patent (Pimentel) includes the IgY immunoglobulins in the yolk and IgM and IgA immunoglobulins in the albumin as taught by Kaspers *et al*. The product by process would inherently have the same property as claimed. Finally, there is no evidence of record that the binding affinity of the IgY immunoglobulin to the colony-forming immunogen being increase by IgM or IgA immunoglobulin. In fact, the specification discloses on page 10, line 4-5 that "the albumin helps resistance to the whole egg preparations and helps protect the avian antibodies."

At paragraph bridging pages 15 and 16 of the Brief, Appellants argue that Pimental ('489 patent) discloses a method for increasing feed conversion efficiency in mammals with a diet containing an antibody produced using the enzyme urease as the antigen. Pimental ('489 patent) states that chicken antibodies are generally known to protect the recipient against bacterial infections. No antibody has been shown to increase feed conversion efficient. Col. 2, lines 59-63. Pimental '489 is limited to the use of an antibody against the enzyme urease to obtain increased feed utilization and body weight gain in animals. There is no teaching in Pimental '489 of a method of promoting the growth of food animals by binding IgY immunoglobulins combined with IgM and IgA immunoglobulins to protein-wasting immunogens to inhibit the ability of the protein-wasting immunogens to adhere to the rumen or intestinal tracts of food animals and to reduce the ability of the immunogens to multiply.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. There is no evidence of record that when administered to the food animal the product produced by the claimed method actually decreases the waste of dietary protein caused by the presence of any protein-wasting immunogen in the rumen or intestinal tracts of any food animals and thereby promoting the growth of the food animal.

In response to appellants' argument that there is no teaching in Pimental '489 of a method of promoting the growth of food animals by binding IgY immunoglobulins combined with IgM and IgA immunoglobulins to protein-wasting immunogens to inhibit the ability of the protein-wasting immunogens to adhere to the rumen or intestinal tracts of food animals and to reduce the ability of the immunogens to multiply, the '895 patent (Tokoro) teaches a method of producing a microbial adherence inhibitor such as a yolk antibody that inhibits the targeted colony-forming bacteria (immunogen) such as *E coli* and the reference IgY antibody is used as an additive to food for animal or as a solution such as milk to livestock to prevent adherence of the targeted immunogen in the intestinal tract of the animal (See column 9, line 42-46, column 10, line 30, column 5 lines 29 bridging column 6, lines 1-49, column 9, lines 43-57, column 10, line 29-31, in particular). Yokoyama *et al* teach a method of producing a microbial adherence inhibitor such as IgY for administration to food animal such as piglets to inhibit the adherence of a targeted colony forming immunogen such as E coli in the intestinal tracts of reference animal (See abstract, in particular). Trinchieri *et al* teach the attachment or adherence of *E coli* to cells is inhibited by IgA (Abstract, in particular).

At page 16 of the Brief, appellants argue that Krause et al does not disclose or suggest that IgY immunoglobulins bind to protein-wasting immunogens and that IgM and IgA immunoglobulins assist and help the binding process. Krause et al discloses that amino acid degradation in the rumen of animals is nutritionally wasteful and produces more ammonia than the bacteria in the rumen can utilize. The excess ammonia is converted by the animal into urea and discharged into the environment as environmental pollution. The feed additive monensin decreases ammonia accumulation in the rumen. Krause et al discovered that monensin inhibited growth of *P. anaerobius* and *C. sticklandii* in the rumen of an animal but did not inhibit *C aminophilium*. The result was the reduction in the amount of ammonia in the rumen and reduction of environmental pollution. There is no teaching that monensin prevents adherence of a targeted immunogen in the intestinal tract of an animal thereby inhibiting its colony growth. Monensin does not promote the growth of food animals by preventing targeted immunogens from adhering to the intestinal tract of an animal. U.S. Patent Nos. 3,501,568 and 3,794,732 are directed to the use of monensin for promoting growth and feed efficiency of food animals. Monensin can be toxic to some animals. Feed intake of the animals is reduced as monensin cannot be added to molasses. Specification, page 4, lines 8-14.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. One cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

In response to appellants' argument that Krause et al does not disclose or suggest that IgY immunoglobulins bind to protein-wasting immunogens and that IgM and IgA immunoglobulins assist and help the binding process, neither the specification disclosure nor the exemplary embodiments provide evidence that the binding process of IgY immunoglobulins to protein-wasting immunogens being assist and help the IgM and IgA immunoglobulins.

Krause *et al* teach the colony-forming immunogens that are responsible for robbing cattle of nutrients are *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* (See entire document, page 820, col. 1, in particular). Krause *et al* further teach adding antibiotic such as monensin as a ruminant feed additive decreases ammonia accumulation in the rumen of cattle and inhibits the growth of monesin-sensitive obligate amino acid-fermenting bacteria such as *P. anaerobius* and *C. sticklandii* but not the number of *C. aminophilium* in livestock (see abstract, in particular). It would have been obvious to one ordinary skill in the art at the time the invention was made to substitute the immunogen such as the *E coli* as taught by the '895 patent (Tokoro) or Yokoyama et al for the *Peptostreptococcus anaerobius, Closteridium sticklandii, and/or Clostridium aminophilium* that are responsible for ruminal amino acid degradation in cattle as taught by Krause *et al* for a method of producing egg antibody such as IgY in the yolk as taught by the '895 patent (Tokoro) and Yokoyama et al and IgM and IgA in the albumin as taught by Kasper et al to inhibit said colony-forming immunogen from adhering to the rumen of the cattle and thereby inhibiting its growth as taught by Tokoro ('895 patent), Yokoyama et al, kaspers, pimental ('489 patent) and Trinchieri et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '489 patent (Tokoro) teaches that antibodies form the spay-dried whole egg are more resistant to degradation by gastric acidity than the purified (IgY yolk fraction) sprayed-dried antibodies (see column 2, lines 35-39, in particular) and egg antibody is particularly advantageous due the fact that the production is simple, efficient and inexpensive (See column 9, line 43-47; column 3, line

19-27). Krause *et al* teach the colony-forming immunogens that are responsible for robbing cattle of nutrients are *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* (See entire document, page 820, col. 1, in particular). Krause *et al* further teach adding antibiotic such as monensin as a ruminant feed additive decreases ammonia accumulation in the rumen of cattle and inhibits the growth of monesin-sensitive obligate amino acid-fermenting bacteria such as *P. anaerobius* and *C. sticklandii* but not the number of *C. aminophilium* in livestock (see abstract, in particular).

At page 17 first paragraph of the Brief, Appellants argue that Trinchierl. et al publication discloses urinary secretory immunoglobulins A used to inhibit bacterial adherence in human urinary tracts. Trinchieri et al do not disclose or suggest a method for promoting growth of food animals by binding IgY immunoglobulins to colony-forming immunogens assisted by IgM immunoglobulins and IgA immunoglobulins to inhibit the colony-forming immunogens from adhering to the intestinal tracts of the animals.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. In response to appellants' arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145. Trinchieri et al demonstrates that immunoglobulin such as IgA binds specifically to colony-forming immunogen such as *E coli* inhibits the *E coli* from adhering to cell.

The '895 patent (Tokoro) teaches method of producing a microbial adherence inhibitor such as a yolk antibody (IgY) that inhibits the targeted colony-forming bacteria (immunogen) such as *E coli* from adhering to the intestinal track of a living being such as livestock (See column 9, line 42-46, column 10, line 30, column 5 lines 29 bridging column 6, lines 1-49, column 9, lines 43-57, column 10, line 29-31, in particular).

Yokoyama *et al* teach a method of producing a microbial adherence inhibitor such as IgY for administration to food animal such as piglets to inhibit the adherence of a targeted colony forming immunogen such as *E coli* in the intestinal tracts of reference animal (See abstract, in particular).

The claimed invention in claims 1, and 5 differs from the teachings of the references only that the method wherein the entire contents of the harvested eggs which include IgY in the yolks, and IgM and IgA in the albumin of the eggs are dried.

The '489 patent (Pimentel) teaches the use of whole egg (albumin and yolk) antibody which include IgY from the yolk and IgM and IgA from the albumin as evident by the teachings of Kaspers *et al* where the antibody can be dried and/or mixed with feed without first isolating the antibody from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular). The '489 patent (Pimentel) further teaches egg yolk antibodies that bind specifically to *E coli, Samonella* and other type of bacteria when administered to animal prevent the bacteria in the gastro-intestinal tract from attaching to the intestinal wall and thereby decreasing the bacterial numbers by prventing bacterial multiplications (see col. 1, line 29-49, in particular). It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce any microbial adherence inhibitor such as antibody from egg as taught by the '895 patent (Tokoro) or Yokoyma et al to colony-forming immunogen such as *E coli* or *salmonella* and supplying the entire contents of the eggs which includes IgY from yolk and IgA and IgM from albumin as taught by the '489 patent to food animals to inhibit the ability of targeted colony-forming immunogen to adhere to the rumen or intestinal tracts of food animals as taught by Trinchieri et al, the '895 patent and the '489 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated with the expectation of success that antibody from the spay-dried whole egg that include IgY from the yolk and IgM and IgA from the albumin are more resistant to degradation by gastric acidity than the purified (IgY yolk fraction) sprayed-dried antibodies as taught by the '489 patent (see column 2, lines 35-39, in particular). One having ordinary skill in the art would have been motivated with the expectation of success to produce microbial adherence inhibitor such as egg antibody because egg antibody is particularly advantageous due the fact that the procedure is simple, efficient and inexpensive as taught by the '895 patent (See column 9, line 43-47; column 3, line 19-27). One having ordinary skill in the art would have been motivated with the expectation of success that the antibodies specific to the particular colony-forming immunogen from the the spay-dried whole egg that include IgY in the yolk and IgM and IgA in the albumin would inhibit the colony-forming immunogen from adhering or attaching to the instestinal wall as taught by the '489 patent

(Pimentel) (see col. 1, lines 29-48, in particular) or a particular cell as taught by Trinchieri et al. The teachings of Krause *et al* pertaining to the particular colony-forming immunogens such as *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* that are responsible for robbing cattle of nutrients (See abstract, page 820, col. 1, in particular), the teachings of '895 patent (Tokoro), the '489 patent (Pimentel) and Yokoyma et al indicating success in generating egg antibody to various colony-forming immunogens as feed additive to administer to livestock to inhibit the ability of the targeted colony-forming immunogen from adhering to its target as taught by the '489 patent and Trinchieri et al would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination *In re Sernaker* 17 USPQ 1, 5-6 (Fed. Cir. 1983), see MPEP 2144.

At page 17 second paragraph of the Brief, Appellants argue that Yokoyama et al publication discloses isolation of antibodies from chicken egg yolk. Immunoglobulin G (IgG) egg yolk was diluted with distilled water and mixed with ethyl alcohol. The mixture was centrifuged. The supernatant which contained the IgG was purified. This process does not disclose or suggest Appellants' method for production of a microbial adherence inhibitor defined in Claims l, 3, 5, 8, 11, 14 and 17. There is no disclosure in Yokoyama et al of IgY, IgM and IgA immunoglobulins with IgY immunoglobulins binding to protein-wasting immunogens to inhibit the ability of protein-wasting immunogens to adhere to the intestinal tracts of animals and the binding process is assisted or helped by IgM and IgA immunoglobulins.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. In contrast to appellants' assertion that Yokoyama et al teach immunoglobulin G (IgG) instead of IgY, it is well known to one of ordinary skill in the immunology art at the time the invention was made that antibody from egg yolk is commonly known as IgY, which is equivalent to IgG found in mammal as evidence by the teachings of the '489 patent (see col. 2, lines 25-28, in particular).

Yokoyama *et al* teach a method of producing a microbial adherence inhibitor such as IgY for administration to food animal such as piglets to inhibit the adherence of a targeted colony

forming immunogen such as *E coli* in the intestinal tracts of the reference animal (See abstract, in particular). The reference method comprises inoculating the hen in or about to reach their egg laying age with the reference colony forming immunogen such as *E coli* (See page 999, Immunization with fimbrial vaccine, in particular), harvesting the eggs lay by the chickens and separating the IgY from the yolk (See page 999, column 2, Separation of antibodies from chicken egg yolk, in particular), drying the separated IgY (See page 1000, column 2, Production of antibody powders by spray drying, in particular) and when administering yolk antibodies to the living being such as neonatal piglets, the yolk antibodies inhibit the adherence of the colony forming immunogen E coli in the digestive tract. In fact, the claimed method step of inoculating female chickens with a particular targeted colony-forming immunogen such as *E coli* is no different than reference teachings.

In response to appellants' argument that there is no disclosure in Yokoyama et al of IgY, IgM and IgA immunoglobulins with IgY immunoglobulins binding to protein-wasting immunogens to inhibit the ability of protein-wasting immunogens to adhere to the intestinal tracts of animals and the binding process is assisted or helped by IgM and IgA immunoglobulins, Yokoyama et al teach IgY immunoglobulins that binds to protein-wasting immunogens such as E coli to inhibit the ability of protein-wasting immunogens to adhere to the intestinal tracts of animals such as piglet (see discussion supra).

The claimed invention in claims 1, and 5 differs from the teachings of the references only in that the method wherein the entire contents of the harvested eggs which include IgY in the yolks, and IgM and IgA in the albumin of the eggs are dried instead of separating the IgY from the yolk.

The claimed invention in claim 3 differs from the teachings of the references only in that the method wherein the colony-forming immunogen is selected from the class consisting of *P. anaerobius*, *C. sticklandii*, and *C. aminophilium*.

The claimed invention in claim 8 differs from the teachings of the references only in that the method wherein the entire contents of the harvested eggs, which include IgY in the yolks, and IgM and IgA in the albumin of the eggs, are dried and the microbial adherence inhibitor wherein the colony-forming immunogen is *P. anaerobius*.

The claimed invention in claim 11 differs from the teachings of the references only in that the method wherein the entire contents of the harvested eggs, which include IgY in the yolks,

and IgM and IgA in the albumin of the eggs, are dried and the microbial adherence inhibitor wherein the colony-forming immunogen is *C. sticklandii*.

The claimed invention in claim 14 differs from the teachings of the reference only in that the method wherein the entire contents of the harvested eggs, which include IgY in the yolks, and IgM and IgA in the albumin of the eggs, are dried and the microbial adherence inhibitor wherein the colony-forming immunogen is *C. aminophilium*.

Kaspers *et al* teach IgG (IgY) is primary immunoglobulin isotype found in the egg yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular).

The '489 patent (Pimentel) teaches the use of whole egg (albumin and yolk) antibody which include IgY from the yolk and IgM and IgA from the albumin as evident by the teachings of Kaspers *et al* where the antibody can be dried and/or mixed with feed without first isolating the antibody from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular). The '489 patent teaches that antibodies have been reported to be more resistant to degradation by gastric acidity when are contained in the spay-dried whole egg (the entire contents) than mere purified sprayed-dried antibodies, i.e. IgY fraction (see column 2, lines 35-39, in particular). The '489 patent further teaches egg yolk antibodies that bind specifically to *E coli, Samonella* and other type of bacteria when administered to animal to prevent the bacteria in the gastro-intestinal tract from attaching to the intestinal wall and thereby decreasing the bacterial numbers by prventing bacterial multiplications (see col. 1, line 29-49, in particular).

Krause *et al* teach the colony-forming immunogens that are responsible for robbing cattle of nutrients are *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* (See entire document, page 820, col. 1, in particular). Krause *et al* further teach adding antibiotic such as monensin as a ruminant feed additive decreases ammonia accumulation in the rumen of cattle and inhibits the growth of monesin-sensitive obligate amino acid-fermenting bacteria such as *P. anaerobius* and *C. sticklandii* but not the number of *C. aminophilium* in livestock (see abstract, in particular).

Trinchieri *et al* teach that the attachment of *E coli* to human uroepithelial cells is inhibited by high level of the IgA (Abstract, in particular).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to substitute the immunogen such as the *E coli* as taught by Yokoyama et al for the *Peptostreptococcus anaerobius, Closteridium sticklandii, and/or Clostridium aminophilium* that are responsible for ruminal amino acid degradation in cattle as taught by

Krause *et al* for a method of producing egg antibody such as IgY in the yolk as taught by Yokoyama et al and IgM and IgA in the albumin as taught by Kasper et al. It would have been obvious to one ordinary skill in the art at the time the invention was made to dry the separated entire contents whole egg (white and yolk) antibody without first isolating the antibodies from the yolk as taught by the '489 patent (Pimentel) since (IgY) is primary the immunoglobulin isotype from the egg yolk while IgM and IgA are mainly found in the albumin as taught by Kaspers *et al* since egg antiobyd such as IgA can inhibit the attachment of bacteria to cell as taught by Trinchieri *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '489 patent (Pimentel) teaches that antibodies form the spay-dried whole egg are more resistant to degradation by gastric acidity than the purified (IgY yolk fraction) sprayed-dried antibodies (see column 2, lines 35-39, in particular). Kaspers *et al* teach IgG (IgY) is primary found in the yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular). Yokoyama et al teach when administered yolk antibodies to *E coli* to the living being such as neonatal piglets, the yolk antibodies inhibit the adherence of the colony forming immunogen E coli in the digest tract. Trinchieri et al teach that the attachment of *E coli* to human uroepithelial cells is inhibited by high level of the IgA (Abstract, in particular). Krause *et al* teach that bacteria such as *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* are responsible for nutrition depletion and the growth of livestock such as cattle (See entire document). It is within the purview of one ordinary skill in the pharmaceutical art to dry any antibody in the form of powder or dry antibody directly onto a carrier prior to administering to livestock as feed additive as taught by the '489 patent (Pimentel), Yokoyama *et al*. The use of whole egg without separation as taught by the '489 patent (Pimentel) inherently includes the IgY in the yolk and the IgM and IgA in the albumin as taught by Kaspers *et al.*

The teachings of Krause *et al* pertaining to the particular colony-forming immunogens such as *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* that are responsible for robbing cattle of nutrients (See abstract, page 820, col. 1, in particular) the teachings of the '489 patent (Pimentel) and Yokoyma et al indicating success in generating egg antibody to various colony-forming immunogens to administer to food animal to inhibit the ability of the targeted colony-forming immunogen from adhering its targeted as taught by the

'489 patent and Trinchieri et al would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination *In re Sernaker* 17 USPQ 1, 5-6 (Fed. Cir. 1983) see MPEP 2144.

At paragraph bridging pages 17-18 of the Brief, Appellants argue that there are no motivating directions or suggestions in these references that would impel one skilled in the art to produce the claimed method. There is no teaching of a method of promoting the growth of food animals by binding IgY immunoglobulins combined with IgM and IgA immunoglobulins to protein-wasting immunogens to inhibit the ability of the protein-wasting immunogens to adhere to the rumen or intestinal tracts of food animals and to reduce the ability of the immunogens to multiply. There are insufficient teachings of the above combined references and no evidence of a motivating force which would impel one skilled in the art to make and use the claimed method for the production of a microbial adherence inhibitor. The numerous rejections of the claims is evidence that one skilled in the art would not determine that it is obvious to use IgY, IgM and IgA immunoglobulins in the entire contents of eggs to bind the IgY immunoglobulins to protein-wasting immunogens to inhibit the ability of the protein-wasting immunogens to adhere to the intestinal tracts of animals. The binding process is assisted and helped by the IgM and IgA immunoglobulins.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. In contrast to appellants' assertion that there is no motivation to combined the references, one having ordinary skill in the art would have been motivated with the expectation of success that antibody from the whole egg would include IgY from the yolk and IgM and IgA from the albumin and antiboyd preparation with albumin is more resistant to degradation by gastric acidity than the purified (IgY yolk fraction) sprayed-dried antibodies as taught by the '489 patent (see column 2, lines 35-39, in particular). One having ordinary skill in the art would have been motivated with the expectation of success to produce microbial adherence inhibitor such as egg antibody because egg antibody production is simple, efficient and inexpensive as taught by the '895 patent (See column 9, line 43-47; column 3, line 19-27). One having ordinary skill in the art would have been motivated with the expectation of success that the antibodies specific to the particular colony-forming immunogen from the the spay-dried whole egg that include IgY in

the yolk and IgM and IgA in the albumin would would the colony-forming immunogen from adhering or attaching to the instestinal wall as taught by the '489 patent (Pimentel) (see col. 1, lines 29-48, in particular) or a particular cell as taught by Trinchieri et al. The teachings of Krause *et al* pertaining to *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* are responsible for robbing cattle of nutrients (See abstract, page 820, col. 1, in particular), the teachings of '895 patent (Tokoro), the '489 patent (Pimentel) and Yokoyma et al indicating success in generating egg antibody to various colony-forming immunogens to administer to food animal to inhibit the ability of the targeted colony-forming immunogen from adhering to its target as taught by the '489 patent and Trinchieri et al would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination *In re Sernaker* 17 USPQ 1, 5-6 (Fed. Cir. 1983) See MPEP 2144.

Rejection of Claims 5, 20, 23 and 26 under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,080,895 (Tokoro et al, of record, Jan 1992; PTO 1449) or Yokoyama *et al* (Infection and Immunity 60(3): 998-1007, March 1992; PTO 892) each in view of Kaspers *et al* (Zentralbl Veterinarmed A 43(4): 225-31, June 1996; PTO 892), US Pat No 5,741,489 (Pimentel et al, of record, April 1998; PTO 1449), Krause *et al* (of record, Appl Environ Microbiol 62(3): 815-21; 1996, PTO 892), and Trinchieri *et al* (Urol Res 18(5): 305-8, 1990; PTO 892) as applied to claims 1, 3, 5, 8, 11, 14, and 17 mentioned above and further in view of US Pat No 4,748,018 (Stolle et al, of record, May 31, 1988; PTO 1449), and Sugita-Konishi *et al* (of record, Biosci Biotechnol Biochem 60(5): 886-8, May 1996; PTO 892).

At paragraph bridging pages 18 and 19 of the Brief, appellants assert that Claim 5 defines a method of production of a microbial adherence inhibitor that inhibits the adherence of a targeted colony-forming immunogen in the intestinal tracts of live beings including animals. This is accomplished by using the entire contents of eggs having the IgY immunoglobulins and IgM and IgA immunoglobulins to promote the growth of the animals by decreasing the waste of dietary protein caused by the presence of protein-wasting immunogens in the intestinal tracts of the

animals. The IgY immunoglobulins bind to the protein-wasting immunogens, which inhibit the ability of the protein-wasting immunogens to adhere to the intestinal tracts of the animals. The binding process is assisted and helped by the IgM and IgA immunoglobulins. Claims 20, 23 and 26 define the method of making the inhibitor as including immunogens Listeria antigen from *Listeria*, Salmonella antigen from *Salmonella* and Campylobacter antigen from *Campylobacter*.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. The "living being" in claim 5 encompasses any animal such as humans. The specification discloses only a method for the production of avian antibody IgY in yolk, IgM and IgA in albumin of the egg for administration to *food animals* such as beef cattle, dairy cattle and diary herds (see summary of invention, page 11, last paragraph of specification, in particular).

In response to appellants' argument that the claimed method involves making the microbial adherence inhibitor using immunogens such as Listeria antigen from *Listeria*, Salmonella antigen from *Salmonella* and Campylobacter antigen from *Campylobacter*, it is noted that the specific "Listeria antigen" from Listeria, the specific "salmonella antigen" from Salmonella and the specific "campylobacter antigen" from *Campylobacter* are not disclosed in the specification. The specification does not teach which particular Listeria antigen from *Listeria*, Salmonella antigen from *Salmonella* and Campylobacter antigen from *Campylobacter* are to be used to inoculate female chickens to produce the egg immunoglobulins. In fact, the specification discloses growing bacteria such as *E. coli* strain 0157:H7 in a specific culture medium to stimulate a particular antigen or adherin such as Veal infusion Agar and Veal infusion Broth for H antigen from E. coli strain 0157:H7 (see page 13 of specification), Brain Heart Infusion is used to stimulate the O antigen from *E. coli* strain 0157:H7 (see page 14 of specification), Tryptic Soy Broth to simulate Whole cell (WC) antigen from E. coli strain 0157:H7 (see page 15 of specification) and Minca medium for A antigen production from *E. coli* strain 0157:H7 (see page 15 last paragraph of specification) and the bacterial lysate (supernatant) is used inoculating female chickens.

At page 19-20 of the Brief, appellants argue that there is no disclosure in Stolle et al ('018) of IgY, IgM and IgA immunoglobulins with IgY immunoglobulins binding to protein-wasting immunogens to inhibit the ability of the protein-wasting immunogens to adhere to the intestinal tracts of animals. Furthermore, Stolle et al ('018 patent) does not disclose or suggest to one skilled in the art that the binding process is assisted or helped by IgM and IgA

immunoglobulins. There is no disclosure in Sugita-Konishi et al of IgY, IgM and IgA immunoglobulins with IgY immunoglobulins binding to protein-wasting immunogens to inhibit the ability of protein-wasting immunogens to adhere to the intestinal tracts of animals and that the binding process is assisted or helped by IgM and IgA immunoglobulins. The Examiner has again failed to show any motivation to combine his references.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

The combined teachings of the '895 patent (Tokoro), Yokoyama et al, Kaspers et al, the '489 (Pimentel), Krause *et al,* and Trinchieri *et al* have been discussed supra.

The claimed invention in claims 5, 20, 23 and 23 differs from the combined teachings of the references only in that the method wherein the colony-forming immunogen is *Listeria, Salmonella* or *Campylobacter.*

The '018 patent *et al* teach colony-forming immunogens such as *Listeria, Salmonella and Campylobacter* are responsible for various conditions such as salmonellitis in mammalian species and IgY antibody is useful for passive immunization. The '018 patent teaches a method of making IgY antibody to colony forming immunogen or combination of immunogen (antigen) such as *E coli, Listeria, Salmonella* and *Campylobacter* (See column 5, lines 1-30, column 6, line 22-25, in particular). The reference antibody is produced by inoculating an egg laying female birds such as the hen in their egg laying age with the reference immunogen or immunogens such as bacterium as *Listeria, Salmonella* and/or *Campylobacter*, wherein the reference immunogens are colony-forming bacteria that are known to cause food borne illness in humans by decreasing an animal's ability to absorb nutrient, allowing a period of time sufficient to permit the production of bird antibody that binds to the targeted immunogens, collecting the egg laid by the hen, purifying the reference antibody and lyophilizing or drying the separated egg antibody (See column 9, lines 17 bridging column 10, lines 1-29, in particular). The '018 patent teaches that the avian antibody is useful for a method of passive immunity (See abstract, in particular).

Sugita-Konishi *et al* teach a microbial adherence inhibitor such as IgY antibody obtained from hens immunized with a mixture of bacteria such as *Salamonella* that is responsible for salmonella enteritidis, the reference IgY microbial adherence inhibitor inhibits the adhesion of

Salamonella to human intestinal cells (Caco 2) in culture (See abstract, and Materials and Methods, in particular).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to substitute the immunogen such as the *E. coli* as taught by the '895 patent or Yokoyama, the bacteria such as *Peptostreptococcus anaerobius, Closteridium sticklandii, and Clostridium aminophilium* as taught by Krause *et al* for the immunogen such as *Listeria, Salmonella* and/or *Campylobacter* as taught by the '018 patent or the *Salamonella* as taught by Sugita-Konishi *et al* for a method of producing a microbial adherence inhibitor such as immunoglobulins from whole egg that includes IgY from the yolk, and IgA and IgM antibodies in the albumin as taught by Kaspers *et al* to *Listeria, Salmonella* and/or *Campylobacter* as taught *by* the '018 patent, Sugita-Konishi *et al* or Yokoyama *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Sugita-Konishi *et al* teach that egg antibody to *Salamonella* inhibits the adhesion of *Salamonella* to human intestinal cells (Caco 2) in culture (See abstract, and Materials and Methods, in particular). The '018 patent teaches *E. coli, Listeria, Salmonella* and *Campylobacter* are responsible for certain condition in mammals and that IgY antibody that binds specifically to colony forming immunogen or combination of immunogen (antigen) such as *E. coli, Listeria, Salmonella* and *Campylobacter* (See column 5, lines 1-30, column 6, line 22-25, in particular) is useful for a method of passive immunity (See abstract, in particular). The '489 patent teaches that whole egg (white and yolk) antibody can be dried and mixed with feed without first isolating the antibodies from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular) and such antibodies have been reported to be more resistant to degradation by gastric acidity when are contained in the spay-dried whole egg as compared to purified sprayed-dried antibodies (see column 2, lines 35-39, in particular). Kaspers *et al* teach IgG (IgY) is the primary immunoglobulin isotype from the egg yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular). It is within the purview of one ordinary skill in the pharmaceutical art to dry any antibody in the form of powder or dry antibody directly onto a carrier prior to administering to livestock as feed additive as taught by the '489 patent (Pimentel), Yokoyama *et al and* The '895 patent (Tokoro).

In contrast to appellants' assertion that there is no motivation to combined the references, the teachings of the '018 patent (Stolle) pertaining to the particular colony-forming immunogens

such as *Listeria, Salmonella and Campylobacter* are responsible for various conditions in mammalian species and IgY antibody is useful for passive immunization, the teachings of Sugita-Konishi *et al* pertaining to the *Salmonella* is one of the opportunsitic bacteria that is responsible for enteritidis and IgY is useful for inhibit the adheresion of *Salmonella* to intestinal cell (see abstract, page 887, col 2, in particular), the teachings of '895 patent (Tokoro), and Yokoyma et al indicating success in generating egg antibody such as IgY to various colony-forming immunogens to administer to food animal to inhibit the ability of the targeted colony-forming immunogen from adhering to its target as taught by the '489 patent and Trinchieri et al and the teaching of '489 patent (Pimentel) pertaining to the use of avian antibody from the dried whole egg which inherently includes IgY in the yolk and IgM and IgA in the albumin as evident by the teachings of Kaspers *et al* would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination *In re Sernaker* 17 USPQ 1, 5-6 (Fed. Cir. 1983) See MPEP 2144.

Rejection of Claims 6, 7, 9-10, 12-13, 15-16, 18-19, and 29-38 under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,080,895 (Tokoro et al, of record, Jan 1992; PTO 1449) or Yokoyama *et al* (of record, Infection and Immunity 60(3): 998-1007, March 1992; PTO 892) each in view of Kaspers *et al* (of record, Zentralbl Veterinarmed A 43(4): 225-31, June 1996; PTO 892), US Pat No 5,741,489 (Pimentel et al, of record, April 1998; PTO 1449), Krause *et al* (of record, Appl Environ Microbiol 62(3): 815-21; 1996, PTO 892), and Trinchieri *et al* (Urol Res 18(5): 305-8, 1990; PTO 892) as applied to claims 1, 3, 5, 8, 11, 14, and 17 mentioned above and further in view of US Pat 6,086,878 (Adalsteinsson et al, of record, Jul 2000, PTO 892) and US Pat No. 4,166,867 (of record, Sept 1979, PTO 892).

At page 20-23 of the Brief, appellants argue that the separated entire contents of the harvested eggs are not dried before they are coated onto the dry feed carrier material. This avoids the reduction of effectiveness of the IgY, IgM, and IgA immunoglobulins caused by the process of drying the entire contents of the harvested eggs. Adalsteinsson et al ('878 patent) disclose a method of administering to animals an effective amount of a gastrointestinal neuro-modulator antibody to neutralize the neuro-modulator. The egg is dried into an egg powder. An example of

drying is spray drying. The dried egg powder can be mixed with animal rations or sprayed directly onto food pellets. Col. 9, lines 31-39. This is a mixing process wherein dry powder is mixed with animal rations which include food pellets. Appellants coat a carrier material with the entire contents of the harvested eggs. The coated carrier material is distributed into the animal feed. The animal feed mixed with the coated carrier material is supplied to the animals. The carrier material is defined in Claims 1 5, 18 and 21 as a group of materials including soybean hulls, rice hulls, corn, cottonseed hulls, distilled dried grain and beet pulp. Betz et al ('867 patent) disclose a method of making horse feed by mixing farinaceous material, proteinaceous material with fibrous materials, adding moisture, drying the mixture, and coating the combination with vegetable oil. The fibrous materials are selected from a group consisting of soy hulls, cottonseed hulls, and rice hulls. The fibrous materials provide structural strength to the feed pellets and effect stool normality. The fibrous materials are not coated with egg antibody. Mixing dry egg powder to animal rations and coating a mixture of animal food with vegetable oil does not suggest to a person skilled in the art to coat a carrier material with IgY antibody as defined in Claims 14, 17 and 20. In view of the absence of a teaching of the claimed drying of antibody yolk and albumin with a dry feed carrier by Betz et al '867 and Adalsteinsson et al '878, it would not have been obvious to a person skilled in the art to make and use the method claimed in Claims 9-10, 12-13 and 15-16. It would not have been obvious to one skilled in the art to develop a method for making a microbial adherence inhibitor including the step of providing a dry feed carrier material and coating the dry feed carrier material with the separated entire contents of the harvested eggs in view of the teachings of the combined references. Further, the Examiner has completely failed to show any motivation to combine either the Tokoro '895 reference or the Yokoyama et al reference each with the six secondary references.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive.

The combined teachings of the '895 patent (Tokoro), Yokoyama et al, Kaspers et al, the '489 (Pimentel), Krause *et al,* and Trinchieri *et al* have been discussed supra.

The claimed invention in claims 6, and 29 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the

colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins.

The claimed invention in claim 7, 9, 12, 15, 18, differs from the combined teachings of the references only in that the method including a dry carrier material, said drying the separated entire contents of said eggs is achieved by coating the dry carrier material with the separated entire contents of said eggs.

The claimed invention in claims 10, 13, 16, 19, 30, 33, 35, 37 differs from the combined teachings of the references only in that the method includes a dry carrier material, wherein the dry carrier material is from a group of materials including soybean hulls, rice hulls, corn, cottonseed hulls, distilled dried grains and beet pulp.

The claimed invention in claims 31 differs from the combined teachings of the references only in that the method wherein the target forming immunogen is from the class consisting of *P anaerobius, C sticklandii, and C aminophilium.*

The claimed invention in claim 32 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins and wherein the immunogen is P antigen from *P anaerobius*.

The claimed invention in claim 33 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins and wherein the immunogen is CS antigen from *C sticklanddi.*

The claimed invention in claim 36 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said

eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins and wherein the immunogen is CA antigen from *C aminophilium.*

The claimed invention in claim 38 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins and wherein the immunogen is *E coli*.

The '878 patent (Adlasteinsson) teaches hyperimmunized spray-dried egg powder can be mixed with food animal feed rations or sprayed to coat directly onto carrier such as food pellets to maintaining sufficient antibody titers (See column 9, lines 37-46).

The '867 patent (Betz) teaches high performance palatable horse feed carrier such as soybean hulls, rice hulls cottonseed hulls provides the fibrous material and cereal grain such as corn and distilled dried grains provides the carbonaceous materials along with nutritional supplement (See column 3, lines 24-26, column 3, lines 10-18, claims of '867, in particular) while beet pulp provides high energy values (See column 2, line 12-13, in particular). The '867 patent teaches soybean hulls, rice hulls and cottonseed hulls provide the fibrous material as animal feed in order to provide adequate structural strength or integrity to the final feed pellets and also to effect stool normality (See column 3, lines 14-16, in particular).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made by coating the dry feed carrier material such as soybean hulls, rice hulls and cottonseed hulls as taught by the '878 patent (Adlasteinsson) and/or the '867 patent (Betz) with the immunoglobulins from the entire contents of said eggs to *E coli, Peptostreptococcus anaerobius, Closteridium sticklandii,* or *Clostridium aminophilium* as taught by the '895 patent (Tokoro), Yokoyama et al, Kaspers et al, the '489 patent (Pimentel), Krause *et al,* and Trinchieri *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated with an expectation of success to mix antibody with food animal feed rations because the '878 patent (Adalsteinsson) teaches that hyperimmunized spray-dried egg can be mixed with food animal feed rations or sprayed to coat directly onto carrier such as food pellets to maintain antibody titers (See column 9, lines 37-46). The '867 patent (Betz) teaches soybean hulls, rice hulls and cottonseed hulls provide the fibrous material as animal feed in order to provide adequate structural strength or integrity to the final feed pellets and also to effect stool normality (See column 3, lines 14-16, in particular). The recitation of coating said dry feed carrier material with the separated contents of the harvested eggs without spray dried is an obvious variation of references teachings since the '489 patent (Pimentel) teach egg antibody from the whole egg (white and yolk) (without first isolating the antibodies) (see col. 2, line 7-8, in particular) can be mixed with carrier such as fine ground corn and then mixed with one metric ton feed (see col. 5, line 1-2, in particular). The '489 patent (Pimentel) further teaches that antibody activity is unaffected when eggs are spray dried (see col. 5, line 22-23, in particular). Further, the step of coating dry feed carrier material with the separate entire content of the eggs in the claimed method does not affect the production of microbial adherence inhibitor (IgY, IgM and IgA) antibodies. None of the rejected claims are drawn to a method of producing feed additive coated with the specific antibody. Trinchieri *et al* teach IgA to *E coli* could inhibit the attachment of *E coli* to human uroepithelial cells (Abstract, in particular). The '895 patent (Tokoro) teaches egg antibody is useful as an additive to food for animal or as a solution such as milk to livestock to prevent adherence of the targeted immunogen in the intestinal tract of the animal (See column 9, line 42-46, column 10, line 30, column 5 lines 29 bridging column 6, lines 1-49, column 9, lines 43-57, column 10, line 29-31, in particular). Yokoyama *et al* teach administering IgY that binds specifically to immunogen such as *E coli* to food animal such as piglets would inhibit the adherence of a targeted colony forming immunogen such as *E coli* in the intestinal tracts of the reference animal (See abstract, in particular).

In response to appellants' argument that the fibrous materials or carrier are not coated with egg antibody, Pimentel ('489 patent) teaches coating carrier such as ground corn with egg antibody (see col. 5, line 1-2, in particular).

Rejection of Claims 20-28 and 38 under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,080,895 (Tokoro et al, of record, Jan 1992; PTO 1449) or Yokoyama *et al* (of record, Infection and Immunity 60(3): 998-1007, March 1992; PTO 892) each in view of

Kaspers *et al* (of record, Zentralbl Veterinarmed A 43(4): 225-31, June 1996; PTO 892), US Pat No 5,741,489 (Pimentel et al, of record, April 1998; PTO 1449), Trinchieri *et al* (of record, Urol Res 18(5): 305-8, 1990; PTO 892), US Pat 6,086,878 (Adalsteinsson et al, of record, Jul 2000, PTO 892) and US Pat No. 4,166,867 (Betz et al, of record, Sept 1979, PTO 892), US Pat No 4,748,018 (Stolle et al, of record, May 31, 1988; PTO 1449), and Sugita-Konishi *et al* (of record, Biosci Biotechnol Biochem 60(5): 886-8, May 1996; PTO 892).

At page 23-24 of Brief, appellants argue that Claims 20, 23 and 26 define a method for the production of a microbial adherence inhibitor by inhibiting the adherence of colony-forming immunogens. The entire contents of eggs having the IgY immunoglobulins and IgM and IgA immunoglobulins are administered to the animals to promote the growth of the animals by decreasing the waste of dietary protein caused by the presence of protein-wasting immunogens in the intestinal tracts of the animals. The IgY immunoglobulins bind to the protein-wasting immunogens which inhibits the ability of the protein-wasting immunogens to adhere to the intestinal tracts of the animals. The binding process is assisted and helped by the IgM and IgA immunoglobulins. The protein-wasting immunogens are identified as Listeria antigen from *Listeria*, Salmonella antigen from *Salmonella* and Campylobacter antigen from *Campylobacter*. Claims 21-22, 24-25, 27-28 and 38 include the step of providing a dry feed carrier material and coating the dry feed carrier material with the separated entire contents of the harvested eggs. The entire contents of the separated eggs are not dried before coating the dry carrier material with said contents of the eggs. The inclusion of a dry feed carrier material and coating the material with the entire contents of harvested eggs is not shown or suggested by the prior art, either alone or in combination. Further, there is no "clear and particular" objective evidence of record showing motivation to combine the myriad references.

Appellants' arguments filed 9/23/04 have been fully considered but are not found persuasive. In contrast to appellants argument that the inclusion of a dry feed carrier material and coating the material with the entire contents of harvested eggs is not shown or suggested by the prior art, Pimentel ('489 patent) teaches coating dried feed carrier such as fine ground corn with egg antibody from whole egg (see col. 5, line 1-2, col. 5, line 54-55, in particular).

The '895 patent (Tokoro) teaches method of producing a microbial adherence inhibitor such as a yolk antibody that inhibits the targeted colony-forming bacteria (immunogen) such as *E coli* from adhering to the intestinal track of a living being such as livestock since the reference

antibody is able to prevent diarrhea that results in wasting of dietary protein. The reference microbial adherence inhibitor is produced by inoculating an egg laying hen in their egg laying age with the reference immunogen such as bacterium *E coli* (See column 5, lines 29-30, in particular), allowing a period of time such as a few weeks after inoculation sufficient to permit the production of bird antibody that binds to the targeted immunogen such as *E coli* (See column 5, lines 47-60, column 6, 10-18, in particular), harvesting the egg laid by the hen (See column 6, line 1, in particular), separating the yolk and albumen (the entire content of the egg) (See column 6, lines 19-20, in particular), drying the separated egg antibody by spray drying or lyophilizing to form powder product (See column 6, line 24-25, in particular). The reference microbial adherence inhibitor such as dried egg antibody is used as an additive to food for animal or as a solution such as milk to livestock to prevent adherence of the targeted immunogen in the intestinal tract of the animal (See column 9, line 42-46, column 10, line 30, column 5 lines 29 bridging column 6, lines 1-49, column 9, lines 43-57, column 10, line 29-31, in particular). The '895 patent further teaches various microbial adherence inhibitors such as egg antibodies produced by the method of inoculating the female bird with immunogens such as K88, K99 and 987P from *E coli* of interest; egg antibody is particularly advantageous due the fact that the procedure is simple, efficient and inexpensive (See column 9, line 43-47; column 3, line 19-27).

Yokoyama *et al* teach a method of producing a microbial adherence inhibitor such as IgY for administration to food animal such as piglets to inhibit the adherence of a targeted colony forming immunogen such as *E coli* in the intestinal tracts of the reference animal (See abstract, in particular). The reference method comprises inoculating the hen in or about to reach their egg laying age with the reference colony forming immunogen such as *E coli* (See page 999, Immunization with fimbrial vaccine, in particular), harvesting the eggs lay by the chickens and separating the IgY from the yolk (See page 999, column 2, Separation of antibodies from chicken egg yolk, in particular), drying the separated IgY (See page 1000, column 2, Production of antibody powders by spray drying, in particular) and when administering yolk antibodies to the living being such as neonatal piglets, the yolk antibodies inhibit the adherence of the colony forming immunogen E coli in the digestive tract.

The claimed invention in claim 21, 24, and 27 differs from the combined teachings of the references only in that the method including a dry carrier material, said drying the separated entire contents of said eggs is achieved by coating the dry carrier material with the separated entire contents of said eggs.

The claimed invention in claims 22, 25, and 28 differs from the combined teachings of the references only in that the method including a dry carrier material, said drying the separated entire contents of said eggs is achieved by coating the dry carrier material with the separated entire contents of said eggs wherein the dry carrier material is from a group of materials including soybean hulls, rice hulls, corn, cottonseed hulls, distilled dried grains and beet pulp.

The claimed invention in claim 38 differs from the combined teachings of the references only in that the method wherein coating said dry feed carrier material with the separated contents of the harvested eggs, said dry food carrier material coated with the entire contents of the said eggs when administered to the living being inhibiting the adherence of colony-forming immunogen in the digestive tract by binding to the IgY immunoglobulins to the colony-forming immunogen, said binding of the IgY immunoglobulins to the colony forming immunogen being assisted by the IgM and IgA immunogloblulins and wherein the immunogen is *Listeria, Salmonella* and *Campylobacter.*

Kaspers *et al* teach IgG (IgY) is primary immunoglobulin isotype from the egg yolk while IgM and IgA are mainly found in the albumin (See abstract, in particular).

The '489 patent (Pimentel) teaches the use of whole egg (albumin and yolk) antibody which include IgY from the yolk and IgM and IgA from the albumin as evident by the teachings of Kaspers *et al* where the antibody can be dried and/or mixed with feed without first isolating the antibody from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular). The '489 patent teaches that antibodies have been reported to be more resistant to degradation by gastric acidity when are contained in the spay-dried whole egg (the entire contents) than mere purified sprayed-dried antibodies, i.e. IgY fraction (see column 2, lines 35-39, in particular). The '489 patent further teaches egg yolk antibodies that bind specifically to *E coli, Samonella* and other type of bacteria when administered to animal to prevent the bacteria in the gastro-intestinal tract from attaching to the intestinal wall and thereby decreasing the bacterial numbers by prventing bacterial multiplications (see col. 1, line 29-49, in particular).

Trinchieri *et al* teach that the attachment of *E coli* to human uroepithelial cells is inhibited by high level of the IgA (Abstract, in particular).

The '878 patent (Adlasteinsson) teaches hyperimmunized spray-dried egg powder can be mixed with food animal feed rations or sprayed to coat directly onto carrier such as food pellets to maintaining sufficient antibody titers (See column 9, lines 37-46).

The '867 patent (Betz) teaches high performance palatable horse feed carrier such as soybean hulls, rice hulls cottonseed hulls provides the fibrous material and cereal grain such as corn and distilled dried grains provides the carbonaceous materials along with nutritional supplement (See column 3, lines 24-26, column 3, lines 10-18, claims of '867, in particular) while beet pulp provides high energy values (See column 2, line 12-13, in particular). The '867 patent teaches soybean hulls, rice hulls and cottonseed hulls provide the fibrous material as animal feed in order to provide adequate structural strength or integrity to the final feed pellets and also to effect stool normality (See column 3, lines 14-16, in particular).

The '018 patent (Stolle) teaches colony-forming immunogens such as *Listeria, Salmonella and Campylobacter* are responsible for various conditions such as salmonellitis in mammalian species and IgY antibody is useful for passive immunization. The '018 patent (Stolle) teaches a method of making IgY antibody to colony forming immunogen or combination of immunogen (antigen) such as *E coli, Listeria, Salmonella* and *Campylobacter* (See column 5, lines 1-30, column 6, line 22-25, in particular). The reference antibody is produced by inoculating an egg laying female birds such as the hen in their egg laying age with the reference immunogen or immunogens such as bacterium as *Listeria, Salmonella* and/or *Campylobacter*, wherein the reference immunogens are colony-forming bacteria that are known to cause food borne illness in humans by decreasing an animal's ability to absorb nutrient, allowing a period of time sufficient to permit the production of bird antibody that binds to the targeted immunogens, collecting the egg laid by the hen, purifying the reference antibody and lyophilizing or drying the separated egg antibody (See column 9, lines 17 bridging column 10, lines 1-29, in particular). The '018 patent teaches that the avian antibody is useful for a method of passive immunity (See abstract, in particular).

Sugita-Konishi *et al* teach a microbial adherence inhibitor such as IgY antibody obtained from hens immunized with a mixture of bacteria such as *Salamonella* that is responsible for salmonella enteritidis, the reference IgY microbial adherence inhibitor inhibits the adhesion of *Salamonella* to human intestinal cells (Caco 2) in culture (See abstract, and Materials and Methods, in particular).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to dry antibody as taught by the '878 patent (Adalsteinsson) by coating the dry feed as carrier material such as soybean hulls, rice hulls and cottonseed hulls as taught by the '867 patent (Betz) with the immunoglobulins from the entire contents of said eggs as taught by

the '489 patent (Pimentel) that contains IgY from the yolk and IgA and IgM as taught by Kaspers *et al* to immunogen such as *E coli* as taught by the '895 patent (Tokoro) or Yokoyama et al, *Listeria, Salmonella* and *Campylobacter* as taught by the '018 patent (Stolle). From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated with an expectation of success to mix antibody with food animal feed rations because the '878 patent (Adalsteinsson) teaches that hyperimmunized spray-dried egg can be mixed with food animal feed rations or sprayed to coat directly onto carrier such as food pellets to maintain antibody titers (See column 9, lines 37-46). The '867 patent (Betz) teaches soybean hulls, rice hulls and cottonseed hulls provide the fibrous material as animal feed in order to provide adequate structural strength or integrity to the final feed pellets and also to effect stool normality (See column 3, lines 14-16, in particular). The recitation of coating said dry feed carrier material with the separated contents of the harvested eggs without spray dried is an obvious variation of references teachings since the '489 patent (Pimentel) teach egg antibody from the whole egg (white and yolk) (without first isolating the antibodies) (see col. 2, line 7-8, in particular) can be mixed with carrier such as fine ground corn and then mixed with one metric ton feed (see col. 5, line 1-2, in particular). The '489 patent (Pimentel) further teaches that antibody activity is unaffected when eggs are spray dried (see col. 5, line 22-23, in particular). Further, the method of coating dry food carrier is an obvious variation of the teachings of the'489 patent (Pimentel) since whole egg (white and yolk) antibody can be dried and/or mixed with feed without first isolating the antibodies from the yolk (see column 2, lines 7-8, column 5, line 52-56, in particular). The '489 patent further teaches that antibodies have been reported to be more resistant to degradation by gastric acidity when are contained in the spay-dried whole egg (the entire contents) than mere purified sprayed-dried antibodies, i.e. IgY fraction (see column 2, lines 35-39, in particular). Trinchieri *et al* teach IgA to *E coli* could inhibit the attachment of *E coli* to human uroepithelial cells (Abstract, in particular). The '895 patent (Tokoro) teaches egg antibody is useful as an additive to food for animal or as a solution such as milk to livestock to prevent adherence of the targeted immunogen in the intestinal tract of the animal (See column 9, line 42-46, column 10, line 30, column 5 lines 29 bridging column 6, lines 1-49, column 9, lines 43-57, column 10, line 29-31, in particular). Yokoyama *et al* teach administering IgY that binds specifically to immunogen such as *E coli* to

food animal such as piglets would inhibit the adherence of a targeted colony forming immunogen such as *E coli* in the intestinal tracts of the reference animal (See abstract, in particular).

In response to appellants' assertion that the binding process is assisted and helped by the IgM and IgA immunoglobulins, there is no evidence of record that the binding process of IgY is assisted and helped by the IgM and IgA immunoglobulins. In fact, the specification on page 10, lines 2-4 discloses that "Once immunized the hen layers the unique IgY types immunoglobulins in the yolk while depositing the common chicken IgM and IgA immunoglobulins in the albumin. The albumin helps resistance to the whole egg preparations and helps protect the avian antibodies."

In response to appellants' assertion that the protein-wasting immunogens are identified as Listeria antigen from *Listeria*, Salmonella antigen from *Salmonella* and Campylobacter antigen from *Campylobacter*,

The specification does not teach which particular Listeria antigen from *Listeria*, Salmonella antigen from *Salmonella* and Campylobacter antigen from *Campylobacter* are to be used to inoculate female chickens to produce the egg immunoglobulin. In fact, the specification discloses growing bacteria such as *E coli* strain 0157:H7 in a specific culture medium to stimulate a particular antigen or adherin such as Veal infusion Agar and Veal infusion Broth for H antigen from *E. coli* strain 0157:H7 (see page 13 of specification), Brain Heart Infusion is used to stimulate the O antigen from *E. coli* strain 0157:H7 (see page 14 of specification), Tryptic Soy Broth to simulate Whole cell (WC) antigen from *E. coli* strain 0157:H7 (see page 15 of specification) and Minca medium for A antigen production from E. coli strain 0157:H7 (see page 15 last paragraph of specification) and the bacterial lysate (supernatant) is used inoculating female chickens. The specification does not disclose the specific medium to culture *Listeria, Salmonella,* and *Campylobacter* to stimulate the expression of which listeria antigen, Salmonella antigen and Campylobacter antigen, respectively.

In response to appellants' assertion that there is no motivation to combine the references, The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles

or legal precedent that some advantage or expected beneficial result would have been produced by their combination *In re Sernaker* 17 USPQ 1, 5-6 (Fed. Cir. 1983) See MPEP 2144.

In this case, the teachings of the '018 patent (Stolle) pertaining to the particular colony-forming immunogens such as *Listeria, Salmonella and Campylobacter* are responsible for various conditions in mammalian species and IgY antibody is useful for passive immunization, the teachings of Sugita-Konishi *et al* pertaining to the *Salmonella* is one of the opportunsitic bacteria that is responsible for enteritidis and IgY is useful for inhibit the adheresion of *Salmonella* to intestinal cell (see abstract, page 887, col 2, in particular), the teachings of '895 patent (Tokoro), and Yokoyma et al indicating success in generating egg antibody such as IgY to various colony-forming immunogens such as *E coli, Salmonella* to administer to food animal, the teachings of the '489 patent (Pimentel) indicating success of using egg antibody from whole egg which contains IgY in yolk and IgM and IgA in albumin as evident by the teachings of Kasper et al, have been used successfully to inhibit the targeted colony-forming immunogen from adhering to intestinal track (see col. 2, lines 49-54, col. 1, line 43-448, in particular), and the entire content of egg antibody can coated on any carrier such as fine ground corn and use as feed additive, and antibody activity is not affected when eggs are sprayed dried (see col. 5, lines 22-23, in particular), the teachings of Trinchieri et al pertaining to the success of IgA to inhibit the attachment of *E coli* to its targeted cells (Abstract, in particular), the teachings of '878 patent (Adalsteinsson) pertaining to use of egg itself containing the desire antibody can be sprayed dry and then mixed with food rations or sprayed directly onto food pellets, the teachings of the '867 patent (Betz) pertaining to the use of feed carrier such as soybean hulls, rice hulls, corn, cottonseed hulls, distilled dried grains and beet pulp as carrier to provide a source of fibrous material would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art, that is production of egg antibody as feed additive to inhibit the adherence of bacteria such as *listeria, salmonella, and campylobacter* in the digestive tract of food animals.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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Conferees
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